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**CASES DISCUSSED IN THE CLINICS OF
GEORGE B. EUSTERMAN**

**RECURRENT GASTRIC ULCER AND ASSOCIATED GASTROJEJUNAL
ULCER IN THE PRESENCE OF CONSTANT GASTRIC ANACIDITY**

Case 1.—A man aged forty-two came to the Clinic first in October, 1922, complaining of "stomach trouble" of about seven years' duration. The patient's father had died from gastric carcinoma. There was an antecedent history of tonsillitis. The patient had had "camp dysentery" and malaria in 1898 while in Cuba, and following this there had been periods of moderate jaundice for several years. In 1915 the appendix was removed and cholecystostomy performed. The local surgeon reported thick, tarry bile and moderate hepatitis. A few months later, bloating, epigastric discomfort, characterized by a feeling of fulness and crowding, occurred from one to two hours before meals, as if the food had remained too long in the stomach. At intervals the patient experienced cramping epigastric pains four or five hours after meals. Food and soda gave little or no relief, but ice cream, pressure over the affected area, or the assumption of a prone position gave relief. The discomfort occasionally awakened him about 1.00 or 2.00 a.m. Sour, fat, and sweet foods were not well tolerated. The symptoms were intermittent, lasting from several days to several weeks, and the spring and fall exacerbations were especially marked. Constipation was habitual, frontal headaches were frequent, and sexual impotence had been noticed for several years. He denied having had venereal disease.

The patient was well nourished, which was attributable to the large amount of ice cream eaten daily because of the relief it afforded. His color was good. There was slight tenderness in the right epigastrium and spasticity of the sigmoid was evident. The first fractional analysis revealed achylorhydria; the second test meal, two days later, showed total acidity 36 and free acidity 20 in the first fraction; gastric content was 170 c.c. There was no roentgenologic evidence of a gastric or duodenal lesion. Dental roentgenograms revealed five devitalized teeth with considerable periapical involvement. The tonsils were small and rather fibrous, and no pus could be expressed from them.

A tentative diagnosis of chronic peptic ulcer, chronic constipation, and dental sepsis was made. The probability that a functionless gallbladder

reflexly might give rise to gastric dysfunction was also considered. The patient was placed in the hospital on a bland, anticonstipation dietary regimen with milk and alkalis between meals. Improvement was marked.

The patient returned in July, 1923. Relief had been satisfactory for about five months, but failure to adhere to the regimen had again brought about marked constipation and recurrence of the gastric symptoms which had been present daily for two months. He had lost 12 pounds. One month prior to his return epigastric tenderness had been marked for several days. The roentgenologic diagnosis of gastric ulcer had been made elsewhere. This was confirmed by examination, the lesion being found on the lesser curvature just above the incisura (Fig. 213). Total acidity was 40, and free



Fig. 213.—Niche of a perforating type of benign gastric ulcer on the lesser curvature above the incisura.

hydrochloric acid 18. At operation excision of a subacute perforating gastric ulcer and gastrojejunostomy were performed.

On the third visit to the Clinic, about a year later, the patient did not complain of pain, but had not gained weight or strength. He complained of occasional soreness to the left of the umbilicus and in the upper right quadrant (the latter with no relation to food), and also of constipation, anorexia, and sleeplessness. Achlorhydria was present. Roentgenologic examination of the stomach was negative and the anastomosis was free; the gallbladder also appeared normal on roentgenologic examination. Improvement was effected by means of a bland, anticonstipation dietetic regimen. Dental infection had not been eliminated.

The patient came to the Clinic for the fourth time in August, 1927, complaining of attacks of distress of two days' duration at intervals of from two to seven days. He stated that sweets disagreed with him, but that sour dishes caused him no distress, while the opposite had been true at the time of the other visits. From fifteen to sixty minutes after meals he had a sense of weakness and nausea, a feeling of fullness and crowding in the lower left epigastrium, and at times he perspired without evident cause. The discomfort lasted for one or two hours as though food had been retained in the stomach. There was lessened appetite, but no regurgitation, emesis, pyrosis, or hemorrhage. Relief followed a sensation like that of food passing out of the stom-



Fig. 214.—Marked regional spasm only is shown. On roentgenoscopic examination there was evidence of an ulcer at the anastomosis, and on the posterior wall of the stomach distal to the anastomosis.

ach. Neither food nor liquids gave relief, but relief still could be induced by posture and pressure. The epigastrium was tender. Four consecutive gastric analyses showed no free hydrochloric acid; however, blood was present. Roentgenologic examination showed a gastrojejunal ulcer along with a second ulcer on the posterior wall of the stomach distal to the anastomosis (Fig. 214). There was a normal cholecystographic response. The dental foci were removed. Green-producing streptococci were cultured from granulomas from the teeth and an autogenous vaccine was prepared. The patient was transferred to the medical wards of the hospital for further observation and treatment. On repeated aspirations of the stomach, whether during

periods of distress or not, persistent achylorhydria was present. Symptoms were relieved, however, by bland diet, frequent feedings, alkalis, and belladonna.

In retrospect, the occasional soreness at the left of the umbilicus present on the third visit was suggestive clinical evidence of inflammation or ulceration at the site of the anastomosis. On the last admission, the subjective sensations of obstruction to the passage of food soon after meals in the left umbilical quadrant, and the intermittent soreness and tenderness on pressure at the same site were reliable clinical confirmation of the roentgenologic evidence of a gastrojejunal ulcer associated with contraction or partial closure of the stoma by inflammation. The diagnosis of associated gastric ulcer was mainly roentgenologic, and while there had not been surgical confirmation, the lesion could be easily seen on fluoroscopic examination at a site remote from the original ulcer. The normal cholecystographic response would seem to exclude the gallbladder as a factor in the complaint. Incidentally, it is unusual to obtain a normal cholecystogram after surgical drainage of the gallbladder, whether or not any symptoms of a cholecystic nature are present. Incision or surgical drainage of the gall causes dysfunction of the organ, as a rule. The extent of periapical infection would lead one to believe that this was the chief factor in the recurrence of ulcer. Since 1925, however, the patient has been under a severe nervous strain; he has smoked excessively and, in other respects, has been irregular in his mode of living.

Those who see a great many gastro-enterologic cases are always interested in the question of gastric acidity in relation to benign ulcer. The school founded by Sippy has many disciples who attribute great importance to increased gastric acidity and secretion coincident with symptoms of uncomplicated peptic ulcer, and who look for relief of symptoms by neutralization or withdrawal of the secretion. I question whether all of us really agree with the laws laid down by Sippy. Recently Palmer, an exponent of this school, in a series of articles in *Archives of Internal Medicine*, has expressed his views concerning the im-

portance of gastric acidity in relation to the symptoms of ulcer. I think there are many cases of chronic peptic ulcer, both duodenal and gastric, in which low acidity is fairly consistent, although it must be remembered that one gastric analysis is no criterion, and it is quite possible that during the time of active symptoms an adequate amount of hydrochloric acid is frequently present. It is curious that when high acidity and ulcer coexist, adequate control of acidity promotes healing and relieves the symptoms in the majority of cases; if symptoms persist or recur after such treatment, the chances are that the lesion is not uncomplicated benign peptic ulcer. However, cases of subacidity and anacidity are seen in which chronic benign peptic lesions are present. A distinction must be made because, if the lesion is gastric, the chances are that it may be syphilitic, tuberculous, or malignant. In cases of duodenal ulcer it is not as necessary to consider the possibility of syphilis, malignancy, or tuberculosis, but rather of healed ulcer or coexisting disease. It is true that in some cases of peptic ulcer, anacidity may be explained by the presence of gallbladder disease, chronic arthritis, pernicious anemia, or some other condition associated with achylia. Clinical experience and experimental studies have shown that the chemical factor is important in retarding healing. I recall a case with characteristic deformity of the duodenal bulb and gastric anacidity on repeated fractional tests; there was no evidence of pernicious anemia or other serious organic disease and the clinical earmarks of chronic anacid gastritis were present. At operation, the surgeon discovered and severed a taut band between the liver and omentum, causing partial stricture of the duodenum proximal to the pylorus. On fluoroscopic examination after operation the duodenal cap was normal. This case is a reminder that there are some clinical criteria, which must be taken into consideration along with the roentgenologic data.

In this case it seemed that early removal of the dental foci might have prevented recurrence. Five per cent of all chronic benign gastric ulcers, usually of the perforating type, are associated with subacidity or anacidity. They occur chiefly in

elderly patients with extensive foci of infection. Cases such as this one are rare, but when they do occur demonstrate the etiologic significance of focal infection more distinctly than the usual type of case.

In the last analysis, it is highly probable that the actual factors which make recurrent ulcer possible in the majority of cases are still unknown. It is reasonable to suppose this to be true on the basis of clinical facts. Why do gastrojejunal ulcers almost always follow gastrojejunostomy for duodenal ulcer, rather than gastrojejunostomy for gastric ulcer? Why is it extremely rare to see anastomotic ulcers following resection of the stomach for gastric carcinoma? Yet following extensive resection of the stomach for benign gastric or duodenal ulcer there is a certain tendency to anastomotic ulceration, even in cases in which achlorhydria has been consistent after operation. To my knowledge there is no satisfactory explanation for these phenomena, yet they lie at the root of the vexing problem of the pathogenesis of chronic ulcer.

HEMOCHROMATOSIS

Case 2.—A man aged thirty-nine first came to the Clinic in February, 1926. He had a wife and two children in good health. He had had gonorrhea in 1907, complicated by a urethral stricture, prostatitis, and "soft chancre," for which he had been treated. In December, 1925 he had had influenza followed by pneumonia. For a number of years he indulged in alcoholic drinks freely at times. Since national prohibition he had resorted to "corn liquor." He smoked cigarettes freely. In January and February, 1924 he was under great strain and worry, lost weight and strength, and was nervous and anemic. He was treated for two months in hospital, and improved considerably, gaining 14.5 pounds. He resumed hard work, alternating between Texas and Oklahoma, and circumstances made living irregular and unhygienic. He became very much fatigued and took a vacation. In the latter half of 1924 and first half of 1925 he felt well. In May, 1925 a mass was found on a casual examination in the upper part of the abdomen. There were no subjective symptoms. Exploration was advised, but not accepted. Roentgenograms showed apparent pressure of the mass on the duodenum. In August a so-called billious attack occurred, characterized by headache, nausea, and sclerotic icterus. It is possible that the abuse of alcohol had something to do with this. From August to November the patient took small doses of bromoseltzer, three or four times a week, because of afternoon headache attributed to the intense heat. During the same period watery

bowel movements, five to six times daily, were attributed to the character of the water in Texas, as the condition was endemic. In November a badly infected tooth was extracted. He then complained of gas after meals and a little belching or bloating. There was no pain. Slight urethral disturbance due to a small stricture was corrected by dilatation. December 15, in Chicago, the patient had a short period of malaise followed by aching in joints, high fever for five or six days, severe cough and expectoration which was not bloody, but rusty. This condition was diagnosed as pneumonia and the patient was confined to bed for two weeks. On arising he found that his clothing was too small at the waist. He improved in health somewhat and returned to Texas the latter part of January, 1926. En route he had another cold, but no fever. He consulted his home physician for "liver trouble." The abdominal distention was attributed to gas. About this time dyspnea, and then edema of the ankles appeared. In February an internist at Oklahoma City diagnosed pancreatic cyst. The dyspnea, "bloating" (ascites) and edema of the extremities were stationary for a period of six weeks. A bluish, almost cyanotic, appearance of the face and neck had been present for seven or eight years, according to the statement made by the brother and wife. The patient said that it had only been present for a year and a half. The brother also was said to have a slightly cyanotic color and an enlarged liver.

General examination showed a marked bluish, cyanotic appearance, especially of the face and neck. The lips were quite red; the buccal mucous membrane and sclerotics showed no pigmented areas. There was a similar, less marked, generalized discoloration of the rest of the body. The patient looked undernourished, and was weak and uncomfortable. There was marked pulsation of the vessels of the neck, the veins appeared engorged, and the bluish appearance of the face was somewhat increased in the reclining posture. The pulse rate was increased, pulse ranging from 108 to 114, and an occasional arrhythmia was noted due to extrasystoles. The heart was enlarged on percussion, the transverse diameter measuring 20 cm., confirmed by the cardiogram. There were no adventitious murmurs, thrills, or retraction of the intercostal spaces. The systolic blood pressure was 100 mm., the diastolic 78. The lower lobes of both lungs gave evidence of passive congestion. The abdomen was moderately distended due to the presence of fluid. Palpation revealed the presence of a firm, somewhat irregular, slightly sensitive mass in the upper, median, and the left quadrant, the borders of which were indistinct owing to the ascites. There was moderate pitting over the sacrum, as well as of the ankles. The prostate was slightly enlarged and tender. Urinalysis of numerous twenty-four-hour specimens revealed constant oliguria, fair concentration (specific gravity averaging 1.020), traces of albumin, occasional hyaline casts and pus cells. Blood urea was 31 mg. There were no abnormal changes in the fundus. On the date of admission the hemoglobin was 75 per cent, the erythrocytes numbered 4,180,000, and leukocytes 4,200, lymphocytes 31 per cent, large mononuclears 1.5 per cent, and neutrophils 64.5 per cent. Examination of several blood smears did not reveal plasmodia. The Wassermann reaction on the blood was negative, both before and after provocative tests. A spectroscopic examination for both sulph-

emoglobin and methemoglobin showed nothing characteristic for either condition. Polycythemia was also excluded. Roentgenoscopic examinations of the organs of the thorax and stomach were satisfactory, with the exception of evidence of enlargement of heart and old interlobar pleurisy. Roentgenograms of the urinary tract were negative. An electrocardiogram revealed a rate of 92, sinus tachycardia, left ventricular preponderance, and an inverted T wave in Leads I, II, and III. Tests of hepatic function were quite satisfactory in view of later developments; the dye retention was slight. Serum bilirubin was 0.7 mg., with an indirect van den Bergh reaction. The carbon dioxid combining power of the blood plasma was 54.1 per cent by volume. The blood chlorids were 660 mg.

The clinical picture first presented was indicative of a disease of the circulatory organs or polyserositis. There was apparent obstruction to return of the venous blood, as evidenced by the positive venous pulsation in the neck, the enlarged heart, cyanosis, ascites, edema, anoxemia, and pulmonary congestion. A most likely pathologic process was that of mediastinopericarditis associated with perihepatitis. In order to make a more satisfactory examination of the upper abdominal mass treatment with merbaphen and ammonium chlorid was instituted. This was followed by marked diuresis, amounting to 8,000 c.c. in the first twenty-four hours, and a loss of 21 pounds within a few days. A second intravenous injection of 2 c.c. of merbaphen five days later resulted in diuresis of 4,000 c.c. The ascites entirely disappeared, within a few days. The mass, which could now be plainly outlined, had the physical characteristics of an enlarged liver, including both the right and left lobes, especially the latter. The splenic edge was just palpable at the left costal border, but the area of splenic dullness extended well upward. With the removal of the ascites signs of circulatory embarrassment were much lessened. The dyspnea and edema had disappeared. Special cardiologic and syphilologic study excluded chronic adhesive pericarditis and syphilis as a factor. The patient was desirous of an exploratory operation, which was not thought justifiable under the circumstances. Another electrocardiogram revealed data identical with those of the first one. The patient decided to return home and re-examination in a few months was recommended. In the meantime, a salt-free diet and daily intake of fluids, restricted to 1,000 c.c., were prescribed.

At the end of June examination showed persistence of the bluish discoloration, and the other symptoms identical with those present on the patient's dismissal. The area of cardiac dullness was considerably decreased.

The patient presented himself at the Clinic for the third time October 4, 1926. For about six weeks or more before this visit he had noticed excessive thirst, increased appetite, and polyuria. He had lost 10 pounds in weight. A specimen of urine had been sent to a commercial laboratory in September and a report on this was received. This specimen contained 8.2 per cent sugar. The examination at the Clinic revealed a large amount of sugar in the urine, 151.67 gm. in the first twenty-four-hour specimen. Blood sugar was high, 0.330 per cent. The diet up to this time had not been restricted. The results of the general examination were the same as at the previous examinations, especially with respect to the liver and spleen. The skin,

however, showed a tendency to bronzing. The heart had returned to normal size. The systolic blood pressure was 104, the diastolic 64. The pulse rate was 90. An electrocardiogram revealed only an inverted T wave in Derivation III. The constant presence of pus cells in the urine was found to be due to rather marked prostatitis.

A diagnosis of hemochromatosis was made; this was based on the discoloration of the skin, enlargement of the liver and spleen, and subsequent diabetes. A biopsy of the skin, taken from the inner portion of the thigh, was made October 16. This showed a considerable amount of hemosiderin, especially in the basal cell layers, around the sweat and sebaceous glands, and in the subcutaneous tissues.

The patient was referred to hospital, where the food intake and sugar output were carefully balanced. On a weighed diet, providing calories 50 per cent in excess of energy requirements for rest (69 gm. carbohydrates, 50 gm. protein, 220 gm. fat, glucose equivalent of 120 gm.) the daily urinary excretion of glucose averaged 46 gm. for four days and the fasting blood sugar was 0.241 for each 100 c.c. Glycosuria was completely checked by the subcutaneous administration of 35 units of insulin a day, and the fasting blood-sugar level fell to 0.194. The diet was then increased to one providing 70 per cent more than the requirement for rest, this addition being tolerated without further insulin. At no time was any difficulty experienced with the digestion of the large amount of fat in the diet.

The body weight began to rise during the period of hospital treatment, and the patient reported by letter, November 24, that he was doing very well. Death occurred at his home January 1, 1927, after an acute illness of four days. The local physician made an antemortem diagnosis of acute pancreatitis, which necropsy did not reveal. It was believed that carelessness in diet or in the use of insulin was responsible for this sudden unfortunate termination.

At necropsy, the tissues were not stained for hemosiderin, and several important organs were not examined microscopically. No evidence of chronic adhesive pericarditis or tuberculosis was found. The heart was normal in size. The spleen was approximately two and a half times average weight, very firm, with capsule unwrinkled. The cut surface neither bulged nor retracted; it was dull, reddish-purple, with interlacing of pearly gray lines. The liver was enlarged to twice normal size, the right lobe extending about 2 cm. below the costal margin, and the left lobe about 5 cm. below the xiphoid process and to the left to the median axillary line. The surface was dull reddish gray, irregular, and had the typical hob-nailed appearance. It cut with considerable resistance, and the cut surface was dull reddish-gray with dense fibrous interlacing lines running throughout. Normal markings were almost entirely absent. Microscopically, the organ showed great increase in dense fibrous connective tissue; although the embalming fluid had almost destroyed the staining properties of the individual cells, the structure and arrangement would indicate an extensive hydropic or fatty degeneration as well as advanced polylobular or interstitial hepatitis. The pancreas revealed an interlobular increase in fibrous connective tissue, almost complete destruction of the islands of Langerhans, a heavy deposit of brown pigment

in the interstitial tissue throughout, and intense infiltration of lymphocytes, endothelial cells, and scattered polymorphonuclear leukocytes in some areas. A diagnosis was made of chronic interlobular pancreatitis.

Hemochromatosis is apparently a rare disease; about 100 authentic cases have been noted in the literature. In view of Mills' pathologic experience at the Boston City Hospital, it would appear that such cases are often only recognized at necropsy, for in a series of seventeen cases only two were diagnosed during life. Certain pathologists regard pigment cirrhosis and the condition clinically known as hemochromatosis or bronze diabetes as identical entities. The pathology in this disease is well defined, but any definite knowledge bearing on etiology and the cause of excess elaboration of pigment (hemofuchsin and hemosiderin) is lacking. The condition rarely occurs in the female sex. It is chiefly a disease of male adult life. Pigmentation of the skin, hepatic cirrhosis, and glycosuria constitute the diagnostic triad. The appellation, "hemochromatosis" (von Recklinghausen), is preferred to that of "bronze diabetes" (Hanot and Chauffard) because diabetes is usually a late symptom, and there are instances in which only pigmentation and hepatic cirrhosis were noted. When glycosuria is present it signifies the involvement of the pancreas in the cirrhotic process, which is the rule. Sprunt has written comprehensively on the subject and reported three cases. This condition must be distinguished chiefly from Addison's disease and argyria. The pigmentation of the skin is more uniform in Addison's disease, and the mucosa is involved; but the liver and spleen are not enlarged and there is no glycosuria. In argyria the appearance of the skin in many respects is not unlike that of hemochromatosis, but the history, clinical course, and pathologic data should easily separate the two conditions.

Generous or excessive indulgence in alcoholic liquor has been regarded as a cause of this disease by many writers. This may have played a rôle in the case reported. Mallory is of the opinion that chronic poisoning with copper is the cause of the disease. He warns against the use of copper vessels which may come in contact with food or drink, especially if they contain

acids of any kind because the metal is so readily dissolved by many of them. This would exclude the use of copper for cooking utensils of any sort, for shakers of cocktails and acid drinks, and for the worms of condensers in stills. Whether or not Mallory's conclusions are correct remains to be proved. The result of the extensive use of private stills now in vogue should help to solve the problem. But copper cooking utensils were as popular in the past as aluminum is today and yet hemochromatosis is still a clinical curiosity. As regards the two yellow pigments present in the lesion (hemofuchsin, and the iron-containing pigment hemosiderin), Parker, Nye, and Mallory have demonstrated that the former is first deposited in the liver and other cells, and in the course of time slowly changes to hemosiderin.

This case presents several features of clinical interest. A brother who was known to have died from hepatic cirrhosis had some pigmentation of the skin. Information concerning exact details of this case was not obtainable, but the coincidence suggests either a common etiologic agent or a familial tendency, more likely the former. The pigmentation in this case may have been of long duration; the wife and relatives maintained that there had been evidence of it for about seven years; the patient was cognizant of it for only one and a half years. The pigmentation was bluish, leaden-black, undoubtedly similar to the type described by Letulle although much less pronounced. Mills states that there are apparently two distinct types of pigmentation: (1) the more characteristic dull gray-brown or dirty brown discoloration of the skin (face, neck, dorsum of the hands, extensor surfaces of the forearms and legs), due to the presence of the hematogenous pigmentation described, and (2) a type due to an increase of melanin in the skin and other organs and tissues of the body in places where it normally occurs. This form of pigmentation is ascribed to injury of the suprarenal glands by the accumulation of the pigment there. In other words, Addison's disease is produced. This case seems to conform more to the second type. The two types of pigmentation ordinarily occur separately but may and do occur together, and

this probably accounts for the variations in the description of the appearance of the skin by various authors. The enlargement of the heart and evidence of myocardial involvement or other abnormality as revealed by the electrocardiogram were special features. *Pari passu* with improvement in portal circulation through removal of the ascitic fluid by merbaphen and ammonium^{III} chlorid, and whatever other salutary effect this treatment may have on hepatic circulation, in addition to a long period of rest in bed, the heart returned to normal size and function. It is evident that in diseases of this kind complicated by ascites, merbaphen and the associated measures are efficient modern therapeutic agents.

Insulin should favorably influence prognosis in the bronzed diabetic type of hemochromatosis. Sprunt says that the diabetes in these cases is usually severe and rapidly fatal. The duration of life after onset of the glycosuria averages about one year. Recent literature reports incidents in which insulin rescued patients from threatened diabetic coma during the course of the disease. Apparently, laxity in treatment or coöperation on the part of the patient in this case caused his sudden death. The improvement during the hospital period was very encouraging. There are cases which run a milder course and in which the sugar tolerance is easily maintained. One of the cases in our series is of this type. Van den Bergh reports a series of five patients with pigmentation, moderate hyperglycemia, urobilinuria, leukopenia, and relative lymphocytosis. He regards these as attenuated and benign forms of bronzed diabetes.

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A STUDY OF THE CAUSE OF JAUNDICE IN FOUR HUNDRED CASES

HOWARD R. HARTMAN

JAUNDICE is the most striking tangible sign of hepatic disease or dysfunction; when present it invariably dominates the clinical and laboratory picture. At times the jaundice may be so slight as to be overlooked, or its very presence doubted. That the yellow discoloration of the skin and sclerotics is caused by bile pigment can be substantiated by the van den Bergh test. Except in latent jaundice and in cases of late or resolving jaundice the extent of the reaction parallels the intensity of the jaundice. The van den Bergh test also serves a useful purpose in differentiating the jaundice of pernicious anemia, hemolytic icterus and obstructive jaundice, and in distinguishing these types from the spurious jaundice of carotinemia. The test is of the greatest practical importance in those cases of obstructive jaundice in which surgical interference is contemplated, as it may reveal with numerical accuracy increase or diminution in the intensity of the jaundice. Although the introduction and application of hepatic functional tests, duodenal drainage and other laboratory methods have been of material assistance and make for diagnostic refinement, they can be regarded only as complementary to time-honored clinical investigation on the basis of a carefully taken case history, physical examination, and observation of the patient.

When the presence of jaundice is proved it becomes an important diagnostic sign in diseases of the biliary tract. It is not pathognomonic of disease of the liver or obstruction to its ducts, although it often occurs in these conditions. To determine just how frequently this was the case and what pathologic process was the cause of the jaundice, 400 records of patients

who were jaundiced at the time of examination were reviewed. It seemed best to accept only the observation of the jaundice made at the clinic rather than to rely on the history of jaundice given by the patient. In some the van den Bergh test was employed, in others it was not necessary. It is not my purpose to discuss here the value of the different kinds of jaundice as diagnostic criteria, but to establish on a percentage basis the fre-

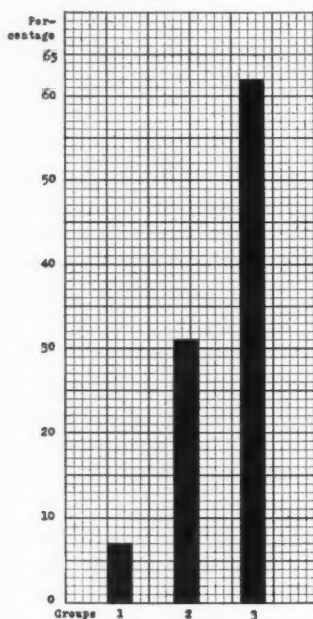


Fig. 215.—Group 1, spleen; group 2, liver; group 3, gallbladder and ducts.

quency of the various pathologic processes that cause jaundice. McVicar and Fitz emphasize McNee's contention that the usual clinical classifications of jaundice are confusing. This contention is well taken. No doubt the terminology in common use to designate the origin of jaundice is as obsolete as that previously applied to digestive disorders. "Gastritis," "dyspepsia," "acute indigestion," and so forth, if used today are not used to

convey the idea of disease entities. Formerly they were so considered. Neither can "catarrhal jaundice," "biliary disease," "toxic jaundice," "infectious jaundice," "familial jaundice," or "hemolytic jaundice" be used intelligently with any assurance that the idea as to the pathologic process or the site of origin of the jaundice will be conveyed to another. It is far better to accept McNee's anatomic classification, in which all types of jaundice are brought under three groups. Group 1 includes jaundice of circulatory or splenic origin; group 2 of hepatic origin, and group 3 of extrahepatic biliary origin. In the series of 400 cases in the light of this classification 7 per cent were of circulatory origin, 31 per cent were of hepatic origin, and 62 per cent of extrahepatic biliary or pancreatic origin. To visualize these figures (Fig. 215, and Table 1) Groups 1 and 2 do not consist strictly of surgical conditions; however, splenectomy is beneficial in cases of hemolytic jaundice, and sometimes cirrhosis is bene-

TABLE 1

ANATOMIC CLASSIFICATION OF 400 CASES OF JAUNDICE	
	Per cent
* Group 1.—Hemolytic jaundice.....	7.00
Group 2.—Catarrhal jaundice.....	11.50
Intrahepatic jaundice*.....	11.25
Carcinoma of the liver (primary and meta- static).....	6.75
Toxic jaundice.....	1.00
Dissociated jaundice.....	0.50
Total.....	38.00
Group 3.—Choledocholithiasis.....	19.75
Carcinoma of gallbladder, ducts, or pancreas.....	17.25
Stricture of common or hepatic ducts.....	9.25
Pancreatitis.....	5.75
Extrinsic pressure on the common duct†.....	4.50
Cholangitis.....	4.00
Inflammatory reaction.....	1.25
Contraction of the common duct.....	0.25
Total.....	62.00

* Including biliary cirrhosis, late stages of portal cirrhosis, and yellow atrophy.

† Caused by edema along the duct, enlarged lymphatics, stones in the gallbladder, empyema of the gallbladder, and so forth.

fited by drainage of the common duct. The conditions in Group 3 are largely surgical and, if there are no contraindications, exploration is justifiable.

Such a gross classification, while interesting and really comprehensive, nevertheless needs explanation to make it practical. Circulatory jaundice, hepatic jaundice, and extrahepatic biliary jaundice can each be produced by a number of pathologic conditions. An analysis of what comprises these groups makes

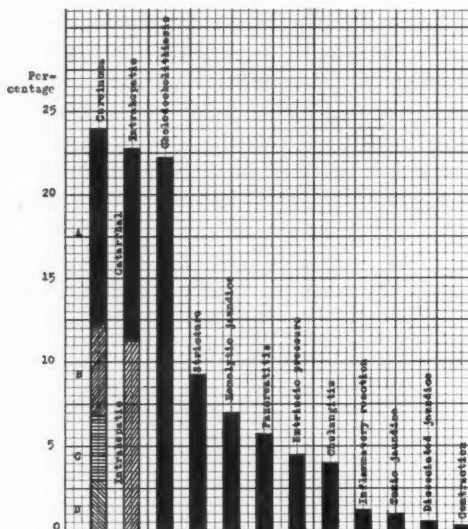


Fig. 216.—A, pancreas; B, gallbladder or ducts; C, metastatic, primary in stomach, rectum, and so forth; D, liver.

this study more illuminating. This necessitates a pathologic division of these anatomic groups. If operation was performed the surgical diagnosis was accepted, otherwise the clinical diagnosis was accepted.

Rearranging the 400 cases of jaundice on a purely pathologic basis shows the relative frequency of carcinoma as a cause of jaundice. It is rather surprising to note that 24 per cent of patients had jaundice because of carcinoma. This indicates

that in general there is practically one chance in four that jaundice is due to malignant disease if the figures here given are representative. In Table 2 (Fig. 216) the situation of malignant growths causing jaundice is given. It will be seen that a malignant lesion in the pancreas accounts for 11.75 per

TABLE 2
PATHOLOGIC CAUSES OF 400 CASES OF JAUNDICE
(Medical and surgical)

Carcinoma:	Per cent
Pancreas.....	11.75
Gallbladder or ducts.....	5.50
Metastatic, primary in stomach, rectum, ovary, and so forth, or general carcinoma.....	3.75
Liver.....	3.00
Total.....	24.00
Intrahepatic:	
Catarrhal.....	11.50
Cirrhosis.....	11.25
Total.....	22.75
Cholelithiasis.....	19.75
Stricture of common or hepatic ducts.....	9.25
Hemolytic jaundice.....	7.00
Pancreatitis.....	5.75
Extrinsic pressure on common duct.....	4.50
Cholangitis.....	4.00
Inflammatory reaction.....	1.25
Toxic jaundice.....	1.00
Dissociated jaundice.....	0.50
Contraction of the common duct.....	0.25

cent of the cases of jaundice in this series; malignant lesion in the gallbladder and ducts for 5.50 per cent; metastatic lesion in the liver for 3.75 per cent, and primary carcinoma of the liver for 3 per cent.

Intrahepatic disease produced jaundice almost as frequently as carcinoma (22.75 per cent). While an attempt was made in this classification to separate the jaundice of the liver from the so-called catarrhal conditions, the folly of doing this is so great that these two conditions were tabulated as one. It is not possible to say that catarrhal jaundice, from occlusion of

the duct due to some inflammatory reaction, is limited to the extrahepatic ducts. More than likely this inflammation of the extrahepatic ducts is only part of the inflammation of the ducts of the liver itself and, therefore, should be classified as an intrahepatic disease along with portal and biliary cirrhosis. Cirrhosis was shown to be the cause of jaundice about as frequently as "catarrhal conditions" (catarrhal 11.50 per cent, intrahepatic 11.25 per cent). According to these figures, gallstones in the common duct occupied third place as a cause of jaundice (19.75 per cent). The other pathologic causes occurred with less frequency (Table 2). Stricture of the ducts, occurring in 9.25 per cent of the cases, was a postoperative condition. Stricture of the common duct and hemolytic jaundice are likely to occur more frequently than any of the other causes of jaundice studied. In series of cases in which more were acute it would be logical to anticipate an entirely different order of frequency of the causes of jaundice. Some reasonable exceptions may be taken to these pathologic diagnoses. Certainly the clinical diagnosis of pancreatitis is always debatable and the surgical diagnosis is not much more accurate. Stricture of the common duct without obvious cause was reported in 9 per cent of the cases by the surgeon and "inflammatory reactions" in the duct caused jaundice in 1.25 per cent. In one case there was contracture of the whole duct from no obvious cause.

This study showed that carcinoma is a most common cause of jaundice and that jaundice of extrahepatic biliary origin occurs almost as often.

THE DIFFERENTIAL DIAGNOSIS OF LESIONS OF THE LOWER PART OF THE ESOPHAGUS AND CARDIAC END OF THE STOMACH

PORTER P. VINSON AND HERMAN J. MOERSCH

In the differential diagnosis of esophageal diseases lesions at the cardia may present unusual difficulties. The evidence obtained in these cases by roentgen-ray examination is too often accepted as final, and the patient is given an unwarranted hopeless prognosis, or a hopeful opinion is ventured when the condition is due to inoperable malignant disease. Only by correlation of clinical evidence with careful roentgen-ray studies and judicious instrumentation can one be reasonably sure of the type of disease present. It is our purpose in this communication to emphasize the points that have been of greatest aid to us in the examination of this type of case.

The most common disease involving the cardia is cardiospasm, the cardinal symptoms being epigastric pain, dysphagia, and regurgitation of food. Pain, which is usually severe, antedates dysphagia by several weeks or months, and when swallowing becomes difficult the pain tends to subside. Dysphagia is constantly present from the onset of the disease, but may vary in intensity. Cold water, apples, popcorn, and effervescing drinks usually cause the greatest difficulty in swallowing.

There may be regurgitation of food and mucus immediately after the patient has eaten, or it may be delayed for many hours. Nocturnal regurgitation is frequently a distressing symptom.

Esophagoscopy examination fails to reveal a significant lesion unless obstruction is marked, and in that case there is usually a severe degree of esophagitis. Such inflammatory reaction is the result of the obstruction and is not a factor in the production of the primary condition.

Roentgen-ray examination usually reveals smooth obstruction at the cardia, but this obstruction may be irregular, due



Fig. 217.—Cardiospasm with filling defect at the point of obstruction.



Fig. 218.—Portion of meat gristle producing irregularity seen in Figure 217.

to the presence of food in the lower part of the esophagus or to unequal muscular contraction (Figs. 217-219). Another point



Fig. 219.—Cardiospasm with irregularity due to uneven dilatation above the cardia.

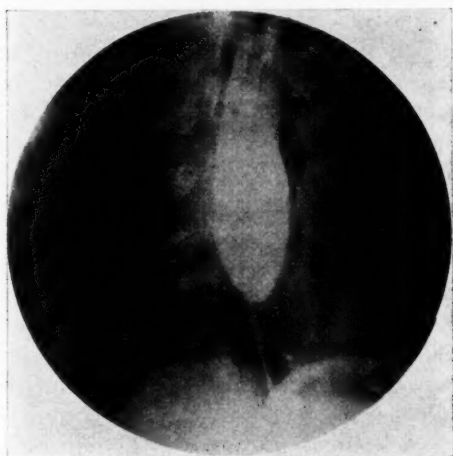


Fig. 220.—Cardiospasm showing obstruction well above the dome of the diaphragm.

that must be borne in mind in the roentgen-ray examination of cardiospasm is that the cardiac end of the esophagus may be above or below the dome of the diaphragm (Fig. 220). The passage of a No. 45 French sound on a previously swallowed thread is accomplished with slight resistance only at the cardia and without bleeding. The symptoms of cardiospasm are usually present for seven years before the patient presents himself for examination. The incidence of men afflicted with the disease seems to be greater than that of women, and it may occur at any age.

Spasm of the esophagus at the cardia may produce symptoms similar to those experienced in cardiospasm. However, the symptoms are more likely to be intermittent and less severe. So far as can be determined by all methods of examination, the esophagus is normal and the diagnosis is made on symptoms alone.

Carcinoma at the cardia may occur primarily in the esophagus, or it may first involve the stomach and produce esophageal obstruction by extension. If the lesion originates in the esophagus, the first symptom is dysphagia of a progressive type beginning with obstruction to solid food and then gradual obstruction to soft food and fluid. Regurgitation is inconstant and is not a prominent feature until obstruction becomes marked. Pain rarely occurs at any stage, and is described as being of a dull, aching type. If the lesion is essentially gastric in origin, the ordinary symptoms of carcinoma of the stomach may be present before the growth infringes on the cardia and produces esophageal obstruction.

On esophagoscopy examination, one may be able to visualize the lesion if it is primarily esophageal, and when this is possible a satisfactory section may be removed for microscopic study. Any one who has had experience in the esophagoscopy examination of lesions at the cardia will readily appreciate the difficulty of obtaining tissue that will reveal the true nature of the disease. If the lesion is in the stomach, it may be impossible to obtain a view of it through the esophagoscope. Roentgen-ray examination is usually quite diagnostic, but a scirrhous carcinoma at the

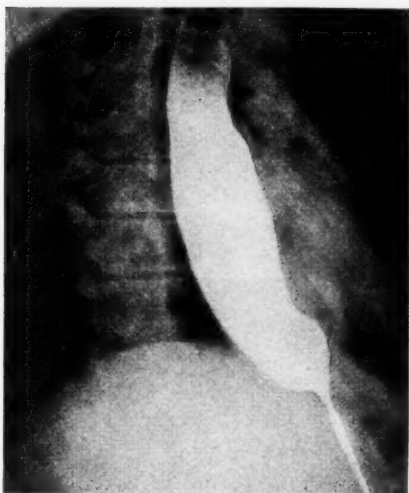


Fig. 221.—Carcinoma at cardia, simulating cardiospasm.

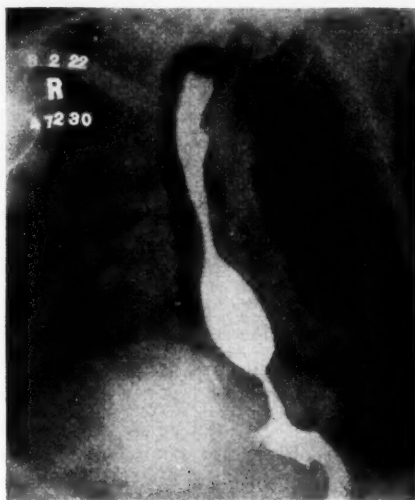


Fig. 222.—Carcinoma of the cardia with smooth obstruction resembling cardiospasm.

cardia may present a smooth obstruction that cannot be distinguished from that produced by a cardiospasm (Figs. 221-223). When sounds are passed, firm obstruction is encountered that may be dilated by using considerable force, which is followed by bleeding. Men are much more often affected with carcinoma at the cardia than women. The disease is seen almost entirely after the age of forty years. The average duration of symptoms is seven months.

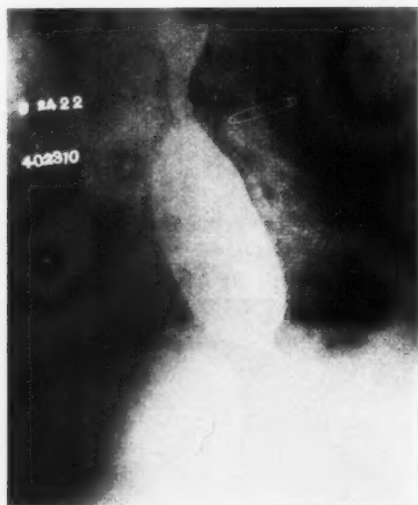


Fig. 223.—Cardiospasm; a striking similarity to Figure 222 may be noted.

Benign ulcer of the stomach rarely, if ever, involves the terminal portion of the esophagus. Although a cicatricial stricture is frequently observed in the lower third of the esophagus, it is exceedingly rare to find such a lesion at the cardia (Fig. 224). The only time we have observed a lesion of this type was in a patient on whom a plastic operation had been performed on the cardia elsewhere for the relief of cardiospasm. The healing of the incision in the esophagus resulted in a cicatricial stricture (Fig. 225).



Fig. 224.—Cicatricial stricture of the lower third of the esophagus.



Fig. 225.—Cicatricial stricture of the esophagus, following plastic operation on the cardia.

Although diverticula just above the cardia are rare they do occur, and it may be difficult to distinguish their manifestations from those of cardiospasm. It is quite likely that they develop because of a mild primary spasm at the cardia. Roentgen-ray examination is our only means of making a diagnosis of this condition (Fig. 226).

An interesting and fairly common lesion that may be distinguished with difficulty from cardiospasm is hernia of the

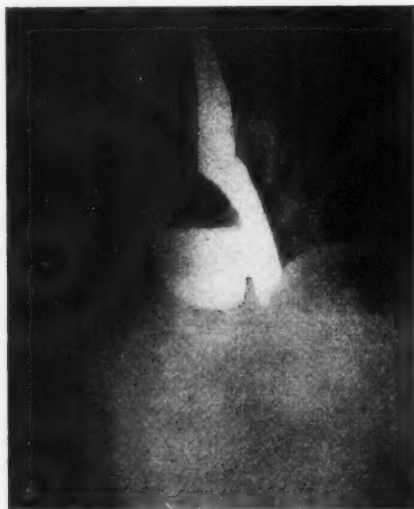


Fig. 226.—Diverticulum of the lower portion of the esophagus.

cardiac end of the stomach through the esophageal opening in the diaphragm. The symptoms of this condition are similar to those of cardiospasm, but with the former the patient suffers more from abdominal distention, especially on lying down.

The dysphagia resulting from pressure on the lower part of the esophagus from the hernial sac is usually relieved by the passage of sounds, but a sense of fulness after meals and pain persist. Careful roentgen-ray studies should be made on all patients suffering from cardiospasm after the cardia has been



Fig. 227.—Unusual type of esophageal obstruction at the cardia, produced by a hernia of the cardiac end of the stomach through the esophageal opening in the diaphragm.

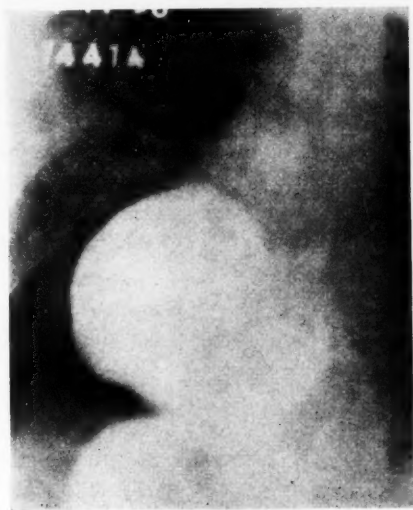


Fig. 228.—Hernia of the stomach filled with barium, same case as shown in Figure 227.

dilated, to rule out the presence of diaphragmatic hernia (Figs. 227, 228).

Diverticula of the cardiac end of the stomach do not cause esophageal obstruction, but do cause distress after meals; the epigastric pain accompanying this condition may be confused



Fig. 229.—Diverticulum of the cardiac end of the stomach.

with similar symptoms in esophageal disease. The roentgen-ray examination is the only one of value in the recognition of this condition (Fig. 229).

CERTAIN PRACTICAL POINTS IN THE ROENTGEN- OLOGIC DIAGNOSIS OF GASTRIC ULCER

ALEXANDER B. MOORE

WHEN a gastric ulcer is revealed by the roentgen-ray as an accessory pocket, or as a niche of considerable size projecting from the lesser curvature in the vicinity of the incisura angularis and is plainly visible in the sagittal view, the diagnosis is obvious and easy. Examples of this sort are striking; they lend themselves well to illustration, and are frequently published, tending to convey the impression that the diagnosis of ulcer can usually be made with facility. Unfortunately for the roentgenologist, such classic cases are in the minority, and routine discovery and identification of gastric ulcer is not a simple problem.

While the common site of ulcers is on or near the lesser curvature, not far from the incisura angularis, a considerable percentage will be found on the posterior wall distant from the curvature, and in any part of the stomach from the cardia to the pylorus. In these situations a projecting niche is seldom demonstrable. Even when situated favorably for observation, the cavity of a small ulcer may be hard to discover. There is thus a rather large proportion of ulcers that are likely to escape detection unless there is some stimulus to an unusually thorough search. It is, therefore, highly important to take note of indirect signs, which are largely due to intrinsic spasm, and of all abnormal manifestations. Among them are narrowing and rolling up of the antrum, gastric retention, hour-glass contraction, and the patient's general appearance which is suggestive of serious disease.

Antral deformity.—Prepyloric narrowing and tucking up of the antrum should always arouse suspicion. It occurs so often in association with ulcers, not only in the pyloric segment but

also remote from the pylorus, that the first thought of the examiner when it is noted should be of ulcer. The lesser curvature is shortened and the narrowed antrum is drawn upward and mesially, so that the stomach assumes an exaggerated fish-hook form. This sign is not new, for it was long ago described by Holzkecht and his pupils as the "snail-form stomach," but is seldom mentioned by American roentgenologists. Because of its frequent occurrence and directive value this sign deserves to be emphasized strongly. Antral deformity may also result from spasm associated with lesions outside the stomach, and tubular prepyloric narrowing may be due to carcinoma, syphilis, or hypertrophy of the pyloric musculature. Hence, deformity with narrowing is not of itself diagnostic, but when it is present an extremely careful search should be made for a niche, which is the sole pathognomonic sign of ulcer. If a niche cannot be found, belladonna should be given and the examination repeated. Spasm from a gastric lesion will persist after belladonna is given to full physiologic effect, while that from extrinsic causes will usually disappear.

Gastric retention.—Another warning index is a residue from the six-hour meal. Ulcer, regardless of its situation in the stomach, is second only to carcinoma in producing gastric retention. Retention may also be due to obstructive duodenal ulcer, but is less frequent, occurs late, and the stomach is dilated, whereas it comes on early in gastric ulcer and the stomach is likely to be small or, at least, not enlarged. Rarely, the accessory pocket of a perforated ulcer will retain barium after the stomach is empty. Whenever gastric retention is noted the niche of a gastric ulcer should be sought, unless other causes are obvious.

Hour-glass contraction.—Hour-glass contraction, either organic or spastic, deserves only passing mention as an index. Ulcer is perhaps its most common cause, but the condition itself is not common. The purely spastic incisura is relatively rare, and it may occur with duodenal ulcer. Certainly, if hour-glass contraction is present, ulcer is to be considered as a possible cause, but the examiner cannot expect it as a frequent signal.

Appearance of the patient.—The general appearance of the patient may have guiding significance to the examiner. As a rule, but with exceptions of course, the patient with gastric ulcer shows the marks of suffering and restricted diet. The presumption is strong that he has an organic lesion. Moreover, the chances are that the lesion is not duodenal ulcer, for with this disease the patient most often has the outward semblance of good health.

Looking for the niche.—To discover a marginal niche it is often necessary to scan closely the gastric outline at various angles and palpate freely during roentgenoscopy, for the crater may be quite small and project visibly at a certain angle only. Palpation directed from the greater curvature toward the lesser curvature aids in outlining the latter margin distinctly. Tenderness to pressure over a doubtful niche is an item of confirmation. In rare instances the niche is on the greater curvature, and inspection of this margin cannot safely be neglected. Roentgenograms made from different directions may assist materially. At the present stage of roentgenology it should not be necessary to warn against mistaking the normal projection on the lesser curvature between two peristaltic waves for a niche. Yet this error is still made too often, especially by examiners who depend on films alone.

Ulcer of the posterior wall.—Carman repeatedly emphasized the necessity of searching for an ulcer on the posterior wall, the crater of which may be recognizable only as a localized dense spot within the shadow of the stomach, the "niche en face." It can be brought into view by stroking manual pressure over the stomach to approximate the anterior and posterior walls and thus thin out the gastric shadow. This manipulation should be commenced early while the patient is drinking the barium mixture. At this time the rugæ are likely to be visible, and their convergence or distortion may aid in finding the crater of an ulcer. Often the niche en face is represented by a mere fleck, and its discovery may be difficult. However small, if it persists or recurs at the same place, it is diagnostic of ulcer.

Prepyloric ulcers.—Identification of ulcers near the pylorus

is most difficult of all. Quite commonly the antrum is distorted on both borders. As in the bulbar deformity caused by duodenal ulcer, it is frequently impossible to prove that any particular marginal prominence is a niche. The deformity is also simulated by extrinsic spasm and by carcinoma. The roentgenologist may be obliged to content himself with the broad diagnosis of "lesion at the outlet." In many cases, however, a fleck can be revealed by pressure, and the diagnosis thus made complete.



Fig. 230.—Ulcer on lesser curvature at the angle of the stomach. A small niche was demonstrable roentgenoscopically. Reflex prepyloric spasm and retraction of antrum may be noted.

The presence of a six-hour residue is valuable confirmatory evidence.

Carcinomatous ulcers.—When its crater is extraordinarily large an ulcer is likely to be malignant, but is not invariably so. Ulcers of the posterior wall surrounded by an elevated ridge and seen roentgenoscopically as a dense area encircled by a translucent zone (Carman's meniscus sign) are the result of ulcerating carcinomas. Otherwise it is impossible to forecast malignancy

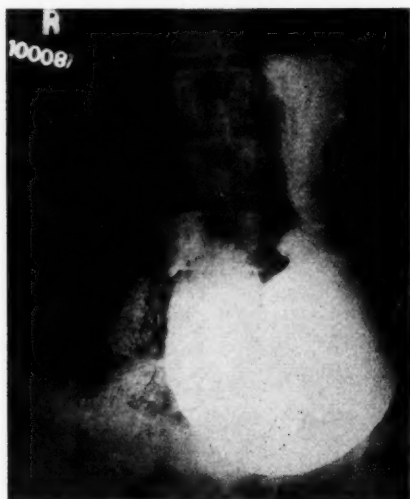


Fig. 231.—Penetrating ulcer on lesser curvature producing a definite marginal niche. Hour-glass contraction of stomach in the plane of the ulcer.

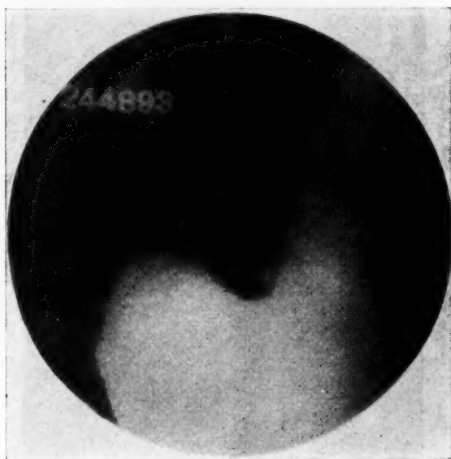


Fig. 232.—Ulcer on lesser curvature with marginal niche, but no incisure or hour-glass deformity.



Fig. 233.—Ulcer with niche, marked prepyloric spasm, and antral retraction.



Fig. 234.—Perforated ulcer, with accessory pocket high on lesser curvature.

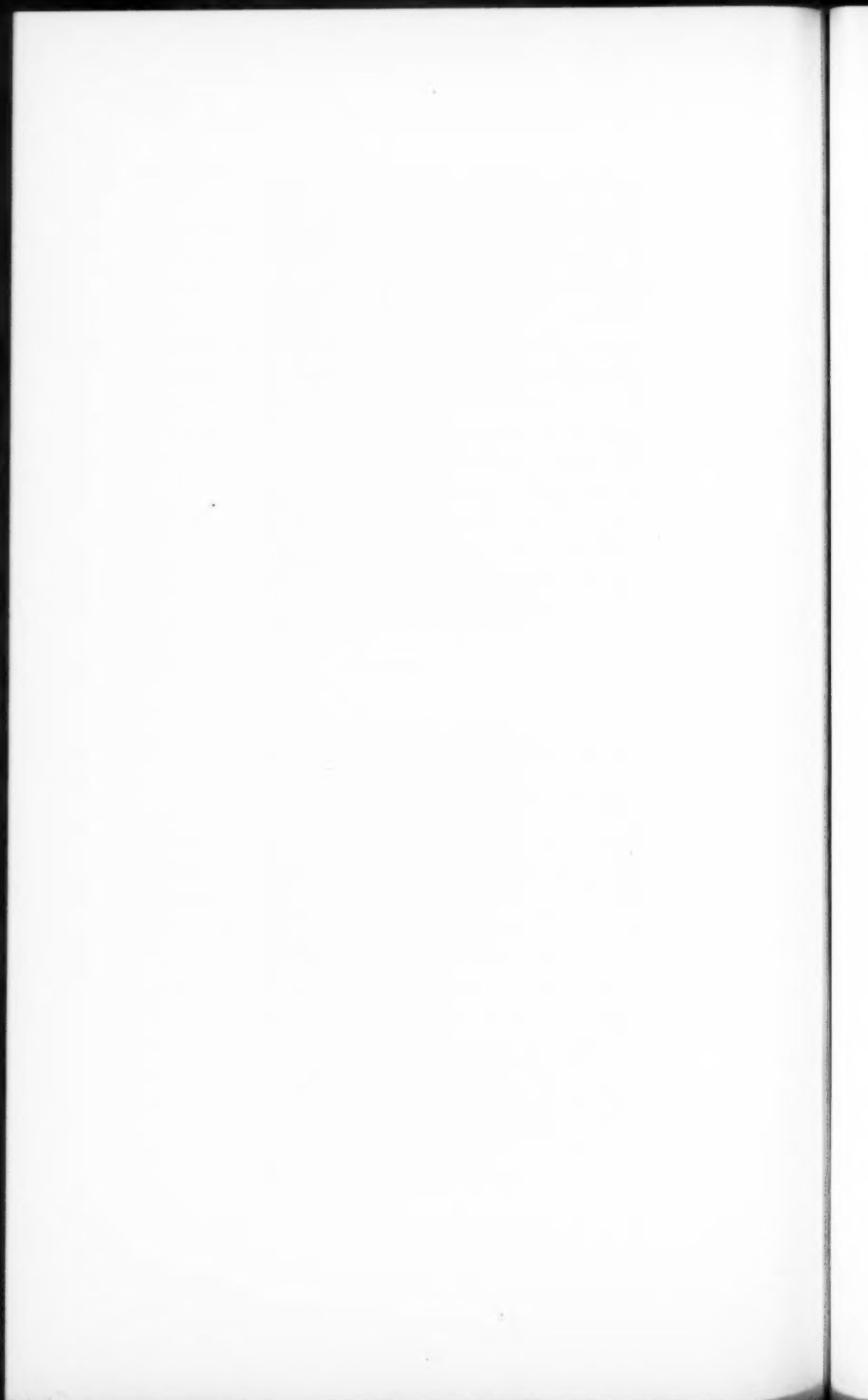
or benignancy, for the smallest fleck-like ulcer may prove to be carcinomatous.

Ulcer following gastro-enterostomy.—Occasionally, after gastro-enterostomy for duodenal ulcer, patients are sent for roentgenologic examination because of recurring symptoms. Gastro-jejunal ulcer is to be considered first, but it must also be borne in mind that a gastric ulcer which was overlooked by the surgeon, or which developed after the operation, may be responsible for the symptoms. It is rather more difficult to discover the ulcer, but the same principles apply as in examination of the stomach on which no operation has been performed.

Localization of ulcers.—The surgeon is sometimes unable to find the site of an ulcer. This applies especially to small fleck ulcers which can neither be seen nor felt from the serous side, and can be exposed only by incising the stomach. If properly construed, the observations made with the roentgen ray will aid in the localization. It is important to remember that the stomach is relaxed, and hence somewhat lengthened by anesthesia. Consequently, an ulcer which on the screen or film appears to be 5 cm. from the pylorus will be found 7.5 or 10 cm. distant in the relaxed stomach.

SUMMARY

The majority of gastric ulcers do not manifest the gross and classic signs depicted commonly in illustrations. Satisfactory diagnosis necessitates alertness for all departures from the normal appearance of the stomach, and thorough exploration in such cases for a niche, with roentgenoscopy and roentgenography at different angles and with other technical aids. Chief among these aids is manual compression to approximate the gastric walls in order to elicit the niche en face, which will be found as often as the marginal niche, if not oftener.



THE PREOPERATIVE TREATMENT OF COMPLICATIONS OF GASTRODUODENAL DISEASE

JAMES F. WEIR

BENIGN ulcer and carcinoma are the gastroduodenal diseases for which the aid of surgery is commonly invoked. Complications, such as perforation, hemorrhage, and obstruction, may arise at any time in the course of these diseases and add to the risk of operative procedures. Berkman (1919 and 1921) demonstrated how adequate preoperative management markedly lowers operative mortality in cases complicated by gastric retention. Since then it has been a policy at the Mayo Clinic, in all cases of complicated gastric disease, to institute a preoperative regimen, the clinical basis and routine of which I shall try to present at this time. Balfour, from the surgical standpoint, has particularly emphasized the importance of this regimen.

With the progress of the disease or the onset of complications preoperative treatment is necessitated by a variety of symptoms: fatigue and pain reduce the patient's recuperative power; retention may induce starvation, dehydration, and toxemia; anemia follows gross or microscopic bleeding. Such unfavorable states are combated by rest, alkalis, and sedatives, by the institution of lavage and proper diet, by the administration of fluid rectally or intravenously, and by transfusion of blood.

In many cases the fatigue of necessary examination is the climax of many nights disturbed by vomiting or hours of pain, varying from moderate distress to the constant agony caused by a perforating lesion. Other patients, especially those of hypersensitive nature, are under mental strain from the anxiety of prolonged disabling disease or the depression that follows the discovery that a malignant process has recently crept on them. A few days' rest, with relief from pain, plenty of sleep,

encouragement and frank discussion of the condition and prospects, will often bring about striking improvement of their physical state and of itself frequently justifies any delay.

Pain may be caused by a perforating lesion or distention of an obstructed stomach by accumulated food and fluid. If the stomach is kept relatively empty by periodic lavage, and bland food is given in small amounts frequently, and if a perforating lesion is treated medically by a suitable diet and the administration of an occasional alkaline powder or a timely sedative, the pain will usually be abolished or so reduced as to be no longer debilitating. Retention from organic obstruction or incompetence of the gastric musculature is the chief local cause of increased surgical mortality; it is to the alleviation of this complication that much of the preoperative care is directed. Nor is the general condition of the patient any more encouraging for he has usually lost considerable weight from restriction of food as a result of loss of appetite or fear of the pain that follows eating. Even if he does eat, the pyloric obstruction prevents food from entering the intestine, and practically no food is absorbed by the stomach. In reality the loss of weight is due to starvation, whether voluntary or involuntary, and the more food that can be absorbed before operation the better. Although there is no hope that the lost weight can be regained before operation, yet, as has been shown in many instances, an adequate reserve of glycogen is an excellent protection in any crisis. In case of retention it is now a routine to give feedings every two hours, commencing at 6.00 a.m. and ending at 8.00 p.m., of 200 c.c. of liquid food, such as strained cereals with sugar and cream, postum with sugar and cream, malted milk, chocolate malted milk, eggnog, or cocoa, made with half milk and half cream, plain ice cream, junket or plain jello with cream, and strained cream soups. Broths or meat extracts and milk are avoided, the former because they stimulate gastric secretion, and the latter because it curdles and may interfere with emptying the stomach by lavage. The diet is nutritious and the quantities given contain 2,500 calories, which can be increased as desired. The stomach is not irritated either mechanically or

chemically, and also the food can be readily evacuated from the stomach.

Lavage is practiced from once to three times daily, depending on the degree of retention or distress. For example, if it is found on two occasions daily that 1,000 c.c. or more is retained, it is much better to empty the stomach three, or even four, times a day. Lavage is timed so as just to precede one of the feedings and not to interfere with any other part of the routine. Emptying of the stomach by this means not only relieves most of the distress, but also removes old accumulated food or barium. It relieves the tension of the muscle of the distended stomach and gives it an opportunity to contract and regain tone. Irritating contents are removed, and any diffuse inflammatory process is placed under optimal conditions for healing. Finally, the patient is accustomed to the use of the tube, which frequently has to be introduced during convalescence.

Dehydration is a more or less constant accompaniment of retention. Dry skin and mouth, thirst, and a small output of highly concentrated urine are the chief clinical earmarks. Consequently, a careful watch is kept of the daily volume of urine. Proctoclysis is more or less of a routine. As a rule, this consists of 1,500 c.c. of 5 per cent glucose solution daily. If obstruction is marked and dehydration consequently severe, from 1,000 to 3,000 c.c. of fluid is given intravenously every day. This method of administration is also often used if proctoclysis is not well tolerated. The intravenous method is gaining greater prominence in the treatment of various lesions. During 1925 there were 2,934 solutions prepared for intravenous use in the Clinic. In 1926 there were 5,684 such solutions made, and thus far, in 1927, approximately 9,671 solutions have been prepared. With proper preparation of the solution and proper technic of administration, untoward reactions are extremely rare and the solutions are used freely.

Another complication associated with gastric retention, either before or after operation, is the so-called toxemia of stasis. This exhausts the patient and alarms the physician and relatives. Before operation such toxemia is noted particularly with high-

grade obstructions. Not infrequently it develops while the patients are under direct observation; it is to be expected when large quantities of material are evacuated from the stomach two or three times daily. Consequently, it is customary to watch closely those chemical changes in the blood (content of sodium chlorid, carbon dioxid, and urea) by which the earliest tendencies to chlorid depletion, alkalosis, and renal insufficiency are manifested. Besides the diagnostic value, such chemical changes are also an index of the results of treatment and should be observed in all cases of retention, the frequency of determination depending on the observations and the degree of obstruction. Solutions containing 10 per cent of glucose and 1 per cent of sodium chlorid are given intravenously freely in amounts varying from 2,000 to 4,000 c.c. daily. Cases have not been seen in which the toxemia could not be controlled either before or after operation. Formerly a more severe and sometimes extremely painful, form of this toxemia was encountered in the form of gastric tetany. It is now approximately two years since I have noted this manifestation. Therapeutically the first indication is to relax the spasms, which can be done by the administration of calcium chlorid (5 c.c. of a 10 per cent solution) intravenously. This must be followed at once by intensive administration of glucose and sodium chlorid solutions, and should be continued until the chemical changes in the blood have been corrected. These factors in the preoperative regimen of pyloric obstruction are illustrated in the following case:

A man aged forty-three, an insurance salesman, had suffered during infancy from typhoid fever, empyema on the right side which had been drained, and an acute abdominal complaint believed to be appendicitis. The trouble had begun in 1913, when he was first observed in the Mayo Clinic. He also came to the Clinic in 1922 and 1927. The pain occurred in spells; the onset was a gnawing discomfort which was relieved for possibly half an hour by food or soda. In one or two days there was severe vomiting. The vomitus consisted of mucus and bile, but was free from food. There was distention. Periumbilical pain followed. Morphin was always necessary for relief. In 1917 an exploratory operation was performed elsewhere, the appendix being removed and adhesions separated without relief. In 1922 the symptoms responded well to treatment for ulcer and the patient was well

for one year, when there was a recurrence with evidence of failing gastric motor function. The use of the stomach tube was begun and afforded temporary relief.

In August, 1927 the patient was again examined. He had lost 30 pounds in weight and much in strength, and large amounts of retained food were obtained by stomach tube. He appeared weak and dehydrated, the voice was husky and the pulse regular, but fast and of small volume. There were signs of old pleurisy at the right base of the lungs, and a moderate succussion splash was noted in the upper part of the abdomen. The systolic blood pressure was 80, the diastolic 68. Gastric analysis showed a total acidity of 74 and free hydrochloric acid 40, in a content of 2,510 c.c. Roentgenograms of the stomach showed duodenal ulcer with marked pyloric obstruction. Preoperative preparation was advised and the patient was admitted to the hospital. Gastric retention decreased, especially in the latter days of preoperative regimen. Intravenous medication was commenced when the blood urea was first found elevated. Larger amounts of solution were injected on the fourth day, when retention increased, the urine output was small, and the patient found difficulty in taking the food offered. The urine output was increased and the disturbance in the blood urea corrected. However, on the fifth day the carbon dioxid combining power was found to be 94 per cent and plasma chlorids 450 mg. Intravenous medication was again increased, now representing approximately three liters. It was continued on the next day, when there was distinct improvement in the condition of the blood, marked reduction in gastric retention, and considerable improvement in the patient's condition clinically, so that he was considered in excellent condition for operation on the seventh day. Gastro-enterostomy was performed. Convalescence was uneventful (Tabulation, page 1412).

This case illustrates the development of mild toxemia with high-grade pyloric obstruction during the patient's preoperative preparation when the stomach was being emptied frequently. On account of the degree of obstruction and great retention we were on the alert for evidence of developing toxemia, and careful study of the blood revealed significant changes which were promptly controlled.

Anemia secondary to gross or microscopic hemorrhage is common in these cases and one must decide when to institute transfusion. If bleeding is acute and severe, transfusion is postponed, if possible, until there has been no bleeding for several days. Then, if the anemia is sufficiently marked, transfusion can be given safely without the danger of again precipitating bleeding. In chronic cases, with hemoglobin below 36 per cent, transfusion is carried out one or more times as seems indicated.

OBSERVATIONS DURING PREOPERATIVE PERIOD IN THE HOSPITAL

Day.	Fluid output, c. c.		Intake, c. c.			Blood.		
	Urine.	Lavage.	Oral.	Rectal.	Intravenous.	Sodium chlorid, mg. per cent.	Carbon dioxide combining power, per cent.	Urea, mg. per cent.
1		1,000		1,500		545	77	48
2		1,050 500	800	1,500	1,000		62	72
3	1,000	1,250	1,000	1,500	1,000			
4	1,000	700 800	800	1,500	2,000			
5	1,500	350 200	1,200	1,500	2,800	450	94	45
6		200 350	1,400	1,500	2,000	575	83	41
7	Operation							

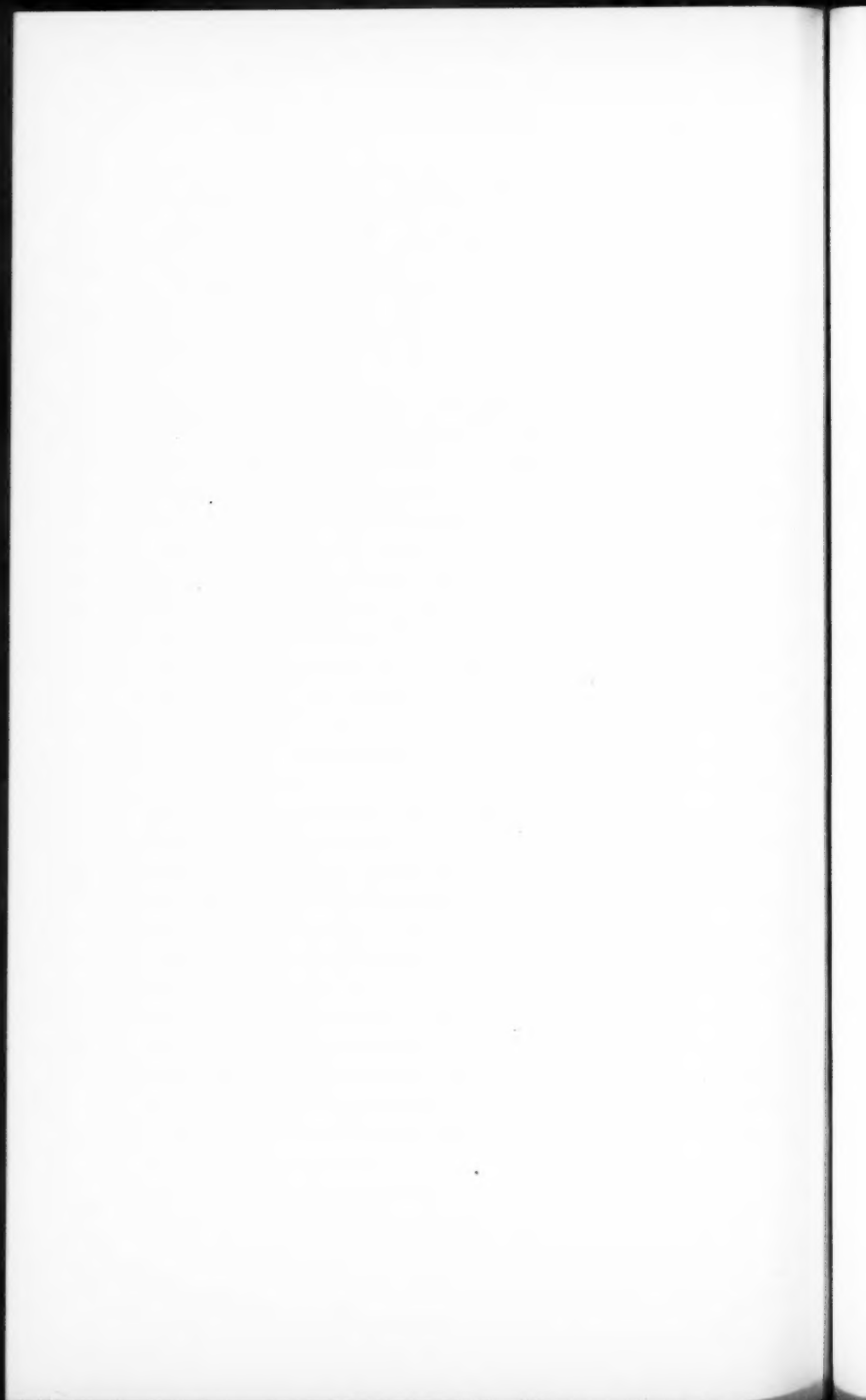
In cases of carcinoma with severe anemia surgical procedures seem to be well tolerated, and transfusion does not appear to raise the hemoglobin content of the blood sufficiently to warrant the procedure except in the most severe cases, and in those in which the chances of resection of the lesion seem good. However, in all these cases the blood grouping should be investigated, so that transfusion can be carried out either immediately or remotely after operation, if the surgeon so desires.

An inflammatory process, sometimes associated with a palpable mass, is occasionally met with, chiefly following perforation of an ulcer; here again preoperative treatment is necessary. Hartman has reported a few such cases. Medical treatment, to allow the inflammation to subside and the exudate to absorb, may make all the difference between nonoperability and operability.

As a rule, from two to four days of preoperative treatment are sufficient. If obstruction is severe and dehydration marked, there is a tendency to prolong the time. The fundamental fault is the obstruction, and it should be relieved as soon as it can possibly be done with safety. Prolonged preparation is fatiguing to the patient, and besides there is the ever-present menace of toxemia. The procedure, therefore, should not be unnecessarily prolonged.

While fatigue, pain, retention, starvation, dehydration, toxemia, and anemia are being combated, the patient should not be kept constantly in bed; he should be urged to be up and around as much as the routine of treatment will permit. Muscular tone and pulmonary ventilation are thus improved and the psychologic atmosphere is less tense. Convalescence is surprisingly satisfactory in these cases and setbacks are rare. If toxemia has been manifested before operation, close watch should be kept for recurrence during convalescence; however, recurrence is unusual. Continuation of adequate intravenous medication usually suffices. The following rules are axiomatic in the treatment of this type of case:

1. Treat cases of complicated gastroduodenal disease preoperatively.
2. Secure adequate fluid intake; the volume of urine should be at least 1,500 c.c. daily.
3. Secure adequate glycogen stores by food of high carbohydrate content, glucose in proctoclysis and intravenous injection of fluids.
4. Give small amounts of food frequently that will readily return through a tube.
5. Empty the stomach sufficiently often.
6. Forestall serious toxemia by frequent examination of the blood for chemical changes, and timely vigorous treatment with glucose and sodium chlorid solutions intravenously.
7. Keep the patient comfortable, physically and mentally.



JAUNDICE ASSOCIATED WITH PERIPHERAL NEURITIS

CHARLES S. McVICAR

Case 1.—A man aged forty-four registered at the Mayo Clinic August 27, 1926. Jaundice was marked and the physical findings indicated diffuse peripheral neuritis. The patient had a tendency to obesity; at one time he had weighed 330 pounds. He was also subject to pains in the joints. On one occasion localization of pain and swelling in the joints of the great toe led to a diagnosis of gout. The attacks of arthritis were usually preceded by a cold in the head. Jaundice was first noted in September, 1925, eleven months before admission, following exposure and a cold. When first questioned the patient could remember only indefinite abdominal soreness, but subsequently recalled several attacks of epigastric pain which had awakened him at night. The jaundice persisted from September, 1925 to March, 1926, when it disappeared for three months; it commenced again in June, 1926 and continued until admission to the Clinic. During the first spell of jaundice he was confined to bed most of the time and lost 110 pounds in weight; he now weighed 130 pounds. The loss in weight up to this time amounted to 200 pounds. In January, 1926, four months after the onset of jaundice, the patient first noticed a burning sensation followed by numbness and tingling in the hands and feet. Foot-drop was noted in July, 1926, and on admission the patient was unable to walk. The muscles of all four extremities were weak and atrophic; most of the deep reflexes were absent, and tenderness was elicited along the nerve trunks and in the atrophied muscle bundles. In the interval between March and June, 1926, when he had become free from jaundice, the patient improved in every way and was almost well. When the jaundice recurred it persisted and the peripheral neuritis progressed.

After a preliminary neurologic examination the patient was placed in the hospital for further study with respect to the jaundice. The urine showed neither arsenic nor lead. He had not used alcohol and had not taken medicine containing arsenic. The blood Wassermann test was negative. Hemoglobin was 63 per cent, erythrocytes numbered 3,510,000, and leukocytes 9,200. The serum bilirubin varied on repeated examinations from 8.6 to 11.2 mg. for each 100 c.c. The van den Bergh reaction was direct. There was no fever. The tonsils were fibrous and pyorrhea was rather marked. Bile was not recovered on repeated duodenal drainage and the stools were acholic. A roentgenogram showed suggestive evidence of gallstones. It was thought that obstruction of the common duct by a malignant tumor could be excluded because the jaundice had disappeared for three months. Intrahepatic jaundice is, as a rule, accompanied by a fairly free flow of bile into the duodenum, at least after a week or ten days. Although the illness was essentially

painless, the history of a few attacks of colic together with the negative results of duodenal drainage and the suggestive roentgenologic report led to a diagnosis of obstruction of the common duct by stone. Operation was advised and undertaken after the usual preoperative preparation.

At operation the gallbladder was found to be subacutely inflamed. It contained several stones and another was found impacted in the common duct at the ampulla. The gallbladder was removed; the common duct was drained and the stone removed. Following operation the jaundice cleared. The patient returned for reexamination October 14, 1927. At this time he weighed 280 pounds, a gain since his last visit of 130 pounds. He could use his upper extremities as well as ever. He could walk fairly well, although foot-drop had persisted to some extent on the right side.

Case 2.—A woman aged forty-one registered September 9, 1927. Commencing seventeen years previously, when the patient was twenty-four, there were rather typical attacks of gallstone colic for a period of three years, but she did not remember whether jaundice followed any of these attacks. She then remained apparently well until September, 1925, when there was a prostrating illness characterized by a sudden onset with vomiting and diarrhea, but without pain. She was confined to bed for six months, during which time well-defined peripheral neuritis developed in the lower extremities. She spent some months in a wheel chair, and gradually recovered the use of her legs, although a certain amount of weakness and subjective disturbance of sensation persisted. In March, 1926, six months after the onset of the acute illness, attacks of colic began, the pain radiating from the right upper quadrant to the back. A short period of jaundice followed each attack.

The patient came to the Clinic because of recurrent attacks of colic. The liver was large and nodular. There was ascites graded 2; the spleen was enlarged; there was no icterus of the skin or sclerotics. The serum bilirubin was not increased in quantity, but gave a direct van den Bergh reaction. The ability of the liver to excrete dye was markedly reduced. Hemoglobin was 66 per cent. A diagnosis was made of gallstones, biliary cirrhosis, ascites, splenomegaly, and secondary anemia.

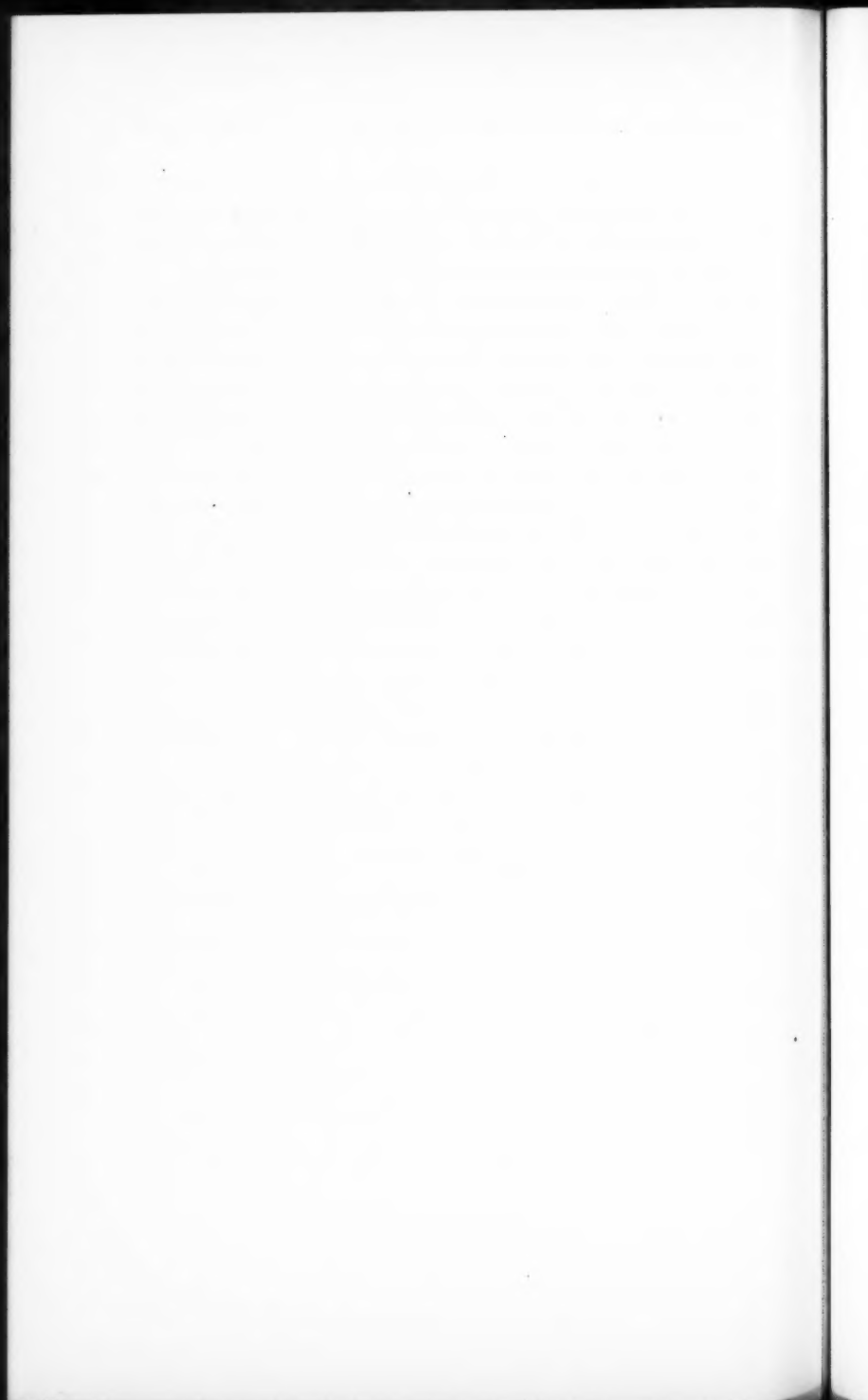
It was considered desirable to have the patient admitted to hospital for treatment of the ascites with ammonium chlorid and merbaphen, but before any special treatment was undertaken the ascites disappeared.

At operation, September 29, a stone, 3.5 by 2.5 cm., was removed from the dilated common duct. A second stone, 2 cm. in diameter, was removed from the gallbladder. The common duct and gallbladder were both drained. Convalescence was uneventful, and the patient was dismissed from hospital nineteen days after operation.

October 22 the abdomen was again swollen. Examination showed ascites, graded 3. The patient returned to the hospital; free diuresis occurred before merbaphen could be administered, although some ammonium chlorid had been given. With this diuresis the ascitic accumulation disappeared.

COMMENT

So far as I know, peripheral neuritis has not been reported as a complication of jaundice, at least in such comprehensive reviews of the subject as those of Murchison or Rolleston. In Case I it seems probable that the gallbladder was an active focus of infection. Focal infection was also present in the teeth and tonsils. The patient did not follow the advice to have these accessory foci removed, but his progress to recovery was satisfactory nevertheless. Case 2 illustrates the aphorism of W. J. Mayo, that "innocent gallstones are a myth," and that it is seldom in the interest of the patient to delay operation for gallstones if skilful operative procedures are available. It also emphasizes the value of studying hepatic function by the dye method when there is no jaundice, and the van den Bergh reaction is qualitatively changed, although the quantity of serum pigment is not increased. The mechanism of the spontaneous disappearance of ascites on two occasions is a matter for speculation. The liver, which was deformed by contraction of scar-tissue, was about twice normal size, presumably because there had been some regeneration of hepatic tissue. The prognosis, after the inciting cause is removed, depends on how much functional compensation had accompanied anatomic overgrowth.



PROBLEMS IN THE TREATMENT OF PATIENTS WITH ASCITES

ALBERT M. SNELL

THE symptom of ascites has been known since the earliest times and apparently was regarded as a clinical entity by the earliest writers; Erasistratus believed it to be an indication of disease of the liver. Galen, in combating this idea, said: "For does it not show the most extreme carelessness to suppose that the blood is prevented from going forward into the liver owing to the narrowness of the passages and that dropsy can never occur in any other way? For to imagine that dropsy is never caused by the spleen or any other part, but always by induration of the liver, is the standpoint of a man whose intelligence is perfectly torpid and who is quite out of touch with things that happen every day." He cites a number of clinical disorders capable of causing ascites; apparently the fact that this condition might be produced by a multiplicity of causes had not escaped this shrewd observer.

In any large series of patients whose presenting complaint is ascites a major group may be distinguished in which the underlying disease may be recognized without particular difficulty from the history and physical examination alone, and a smaller group in which the differential diagnosis may be an extraordinarily complex problem. Any clinician of experience can recall numerous diagnostic errors in this field; even so common a cause of ascites as portal cirrhosis may sometimes escape recognition. It is the practice in the Mayo Clinic to place all patients suffering from ascites in the hospital for observation and study; thus useful points in the differential diagnosis and treatment of ascites have been brought out.

Cabot (1912), in reviewing the necropsy records of the Massachusetts General Hospital from 1870 to 1910, found that the four common causes of ascites were, in order of frequency, cardiac weakness, renal disease, hepatic cirrhosis, and peritoneal tuberculosis. Intestinal obstruction, ovarian tumors, and malignant disease, involving either the abdominal lymph nodes, peritoneum, or liver were next in order; the latter accounted for ascites in about 6 per cent of the cases. Visceral syphilis and adherent pericardium were among the minor causes. Improved methods for the detection of syphilis introduced during the last fifteen years, and the apparent increased prevalence of malignant disease in the same period, necessitate a slight revision of statistics for present day use, but the nine conditions mentioned certainly account for most of the cases of ascites encountered.

Among recently developed procedures that have been of assistance in the diagnosis and treatment of ascites tests of hepatic function are prominent. While disease of the liver without jaundice is not necessarily accompanied by the retention of bromsulphthalein or related compounds, at least 90 per cent of patients suffering from ascites due to hepatic disease have dye retention of considerable degree, a fact well established by operative and necropsy data and serving to orient the clinician in his preliminary survey of the case. A negative dye test, while not positively excluding hepatic disease, serves to focus attention on other possible causes of ascites, while markedly positive tests serve to narrow the field considerably; slight retention of dye (graded 1) often may be taken to indicate secondary hepatic involvement such as one finds in polyserositis (capsular cirrhosis) or in cardiac decompensation (cardiac cirrhosis). In the matter of prognosis the dye tests are of some value, and in the determination of surgical risk when splenectomy or omentopexy is under consideration, the tests give information of great value to the surgeon which is not obtainable by other means.

Another point of interest is the value of the newer diuretics, such as ammonium salts and merbaphen, in the management of

ascites. Their therapeutic efficacy has been discussed by Rown-tree, Keith, Barrier, and others. That a "therapeutic test" may give valuable clues in the diagnosis and prognosis of ascites is not so well known. The quantitative response to such treatment, the contour and appearance of the abdomen during treatment, and the subjective condition of the patient following diuresis caused by merbaphen may afford information which will materially assist in the further treatment of the case. This point is illustrated in the following case:

Case 1.—A woman aged twenty-two came to the Mayo Clinic in March, 1927, complaining of enlargement of the abdomen. The family history was negative and she had always been well prior to December, 1926. She had had one normal pregnancy and the child was two years old. The ascites appeared to have developed rather suddenly three months previously, although on questioning the patient remembered a rather indefinite abdominal distention for a considerable period. At first she had felt abnormally fatigued and also had had night sweats for a brief period. Her physician had found a slight afternoon temperature on several occasions. Abdominal paracentesis had been performed twice, the first being productive of about 250 c.c. of straw-colored fluid, the second of about 3,500 c.c. of viscid, bloody liquid. The patient's general health apparently had suffered little; she appeared to feel quite well except for the marked distention of the abdomen.

The patient was well developed and well nourished; the heart and lungs were normal; the systolic blood pressure was 110, the diastolic 60. The abdomen was distended with fluid, but collateral circulation could not be made out. There was no edema of the extremities. Pelvic examination was unsatisfactory because of severe ascites. Urinalyses, blood count, blood Wassermann tests, renal functional studies, and glucose tolerance tests were carried out, with negative results. Roentgenograms of the chest and spine were negative. The serum proteins were 8.8 gm. per cent and the total blood fats were 243 mg. A test of hepatic function with bromsulphthalein did not show dye retention.

Because of the indeterminate nature of the case the patient was placed in hospital for further study and the trial of combined ammonium chlorid and merbaphen treatment. A diet with low salt and fluid content (as devised by Smith and Keith) was prescribed and 6 gm. of ammonium nitrate given daily. Two doses of merbaphen, 0.5 and 0.75 c.c. respectively, were given at three-day intervals. Each dose produced definite but slight diuresis, and the abdomen became much softer, while the weight decreased about 6 pounds, presumably due to the loss of fluid. On reexamination the upper part of the abdomen and the flanks were tympanitic and a large dome-shaped fluctuant mass occupied the middle part of the abdomen. The gynecologic consultant suspected the presence of a large ovarian cyst or other pelvic tumor. Because of this possibility, as well as that of tuberculous peritonitis, exploratory lapa-

rotomy was performed. The peritoneum was found to be gray and thickened, and there were large bands of adhesions which separated the ascitic fluid into a number of individual collections. Exploration of the pelvis showed that both fallopian tubes were definitely involved in a caseating tuberculous process. Microscopic examination of the peritoneum and tubes showed tuberculosis.

Convalescence was stormy, the patient having a daily fever and severe sweats. She recovered subsequently and was dismissed to carry out a modified heliotherapeutic regimen at home.

The limited response to diuretics in this case and the appearance of the abdomen after a few days' treatment led directly to the proper procedure, that is, exploratory laparotomy. Heart failure, nephrosis, and hemochromatosis could be readily excluded; the age of the patient and the absence of dye retention and collateral circulation made hepatic cirrhosis unlikely. This narrowed the diagnostic field to a consideration of ovarian tumor or cyst, tuberculous peritonitis, and carcinomatosis, the ascites associated with these conditions responding only in a limited degree to the type of diuretic treatment just mentioned.

The appearance of the abdomen with its rounded asymmetric contour was particularly noted. When ascitic fluid lies free within the peritoneal cavity the abdomen is rounded only when it contains a great deal of fluid or is under tension. If a portion of the fluid is withdrawn by paracentesis or "medical tapping," the abdomen flattens and bulges laterally when the patient is in the dorsal position. The general contour is that of a frog's abdomen and the term "batrachian abdomen" has been used to describe it. This rather elementary consideration mentioned in older writings on ascites has been the means of avoiding many mistakes in the treatment of ascites. If the abdomen does not assume the batrachian contour after diuresis, one can be reasonably certain of the presence of encysted fluid or of a peritoneum sufficiently thickened to sustain the ascitic fluid against the force of gravity. The two conditions most commonly capable of causing such a thickened peritoneum are, of course, tuberculosis and carcinomatosis; encysted fluid may also be found in the former condition, as it was in this case. Once the clinician can be certain that the fluid is not free in a normal

or relatively normal peritoneal cavity, the treatment with diuretics may be discontinued and the surgical aspects of the case considered.

A number of cases observed at the Mayo Clinic might be cited to enlarge on the value of observing the abdominal contours during diuretic treatment. Two cases were noted particularly; in one, the patient responded extraordinarily well to merbaphen, but there was marked asymmetry of the abdomen with the left flank prominent. While the advisability of exploration was being considered the patient died suddenly from pulmonary embolism. At necropsy extensive peritoneal carcinomatosis was found. In the second case the response to diuretics was only moderate, a dome-shaped contour of the abdomen persisting in spite of loss of fluid. At exploration a large thin-walled ovarian cyst, together with considerable free ascitic fluid, was removed. It may be noted that in these cases simple inspection of the abdomen furnished information which was not obtainable by palpation or other methods of examination.

It has been said that in any large group of cases of ascites about two-thirds could be classified without particular difficulty, the remaining third presenting a much more difficult problem. Among these obscure and puzzling cases may be mentioned those of adherent pericardium, chronic pleuritis, mediastinitis, perihepatitis, and the various forms of nontuberculous chronic peritonitis. These cases have been grouped under the convenient heading "multiple serositis." In many such instances the diagnosis must be made by exclusion, the clinical criteria being difficult to establish since the underlying lesion is variable and imperfectly understood. The following case is presented not because of the difficulty in diagnosis, but rather to call attention to the possibilities of treatment with the diuretic remedies mentioned as an acceptable substitute for abdominal paracentesis so frequently required in ascites from this cause.

Case 2.—A woman aged twenty-nine came to the Mayo Clinic in October, 1925. She had never been particularly well and for about thirteen years had noticed "bloating" of abdomen which appeared and disappeared without apparent cause. In 1906 right pleural effusion had necessitated paracentesis.

She was married in 1922, but had never been pregnant. Her primary reason for seeking medical advice was an accumulation of fluid in the abdomen which had first appeared in 1923. An exploratory laparotomy performed elsewhere shortly after the ascites was first noted revealed chronic peritonitis, suspiciously like that due to tuberculosis, but a positive diagnosis was not established. Slight cirrhotic changes were noted in the liver and the retro-peritoneal lymph nodes were enlarged. Abdominal paracentesis had been performed about thirty-five times in the two years prior to admission. There had been but slight edema of the extremities and practically no other complaints.

Physical examination revealed a small frail woman with deep pigmentation of the skin of the trunk from ultra-violet light. Marked ascites was present, but collateral circulation could not be demonstrated. A firm liver edge was felt just below the costal margin; the spleen was not palpable. There was definite dullness of both lung bases posteriorly; Litten's sign could not be made out on either side. Examination of the heart was essentially negative except for a faint precordial systolic murmur. The systolic blood pressure was 95 and diastolic 68. Urinalyses, blood Wassermann tests, blood counts, and tests of renal function were negative. A phenoltetrachlorophthalein test for hepatic function showed dye retention graded 1. The serum bilirubin was normal in amount. Roentgenograms of the chest were negative except for definite calcification of the pericardium. The patient presented a letter from her local physician stating that many tuberculin tests and guinea-pig inoculations from the ascitic fluid had been made, with negative results.

Since the patient was anxious to avoid further tapping of the abdomen she was placed on a weighed diet with restriction of inorganic salts and fluid. Ammonium chlorid was given in daily doses of 9 gm. and a trial dose of 0.5 c.c. merbaphen was administered subcutaneously. There was no untoward reaction and three subsequent doses of 2 c.c. were given intravenously, each producing marked diuresis. Dullness at the lung bases could not be demonstrated at the time of dismissal, but a faintly positive Broadbent's sign was noted.

The patient has remained under observation for two years and ascites has not recurred. She has restricted fluid and salt intake moderately, but has taken no medicine. She is now in fairly good health and able to perform her household duties without undue fatigue.

This case represents a fairly good example of so-called multiple serositis, known also as Pick's or Concato's disease, a rare and obscure syndrome that has been the subject of much controversy since its description by Concato (1881), Curschmann (1884), and Pick (1896). The first description in literature is that of Van Deen (1848). As has been stated, there is no agreement as to the fundamental cause of the condition, and the clinical criteria are far from definite. Apparently a variety

of related syndromes have been conveniently grouped under this name; for example, a group of symptoms of tuberculous origin, and others following rheumatic fever. Some cases are primarily the result of chronic peritonitis, others are secondary to pericarditis or pleuritis. The hypothesis that particulate matter may pass freely through the central tendon of the diaphragm (as claimed by Clark and others) has been used by Kelly to explain the mechanism of the spread of the infection as well as the progress and site of the pathologic process. More recent work has raised a doubt with regard to this hypothesis, but nothing better in the way of explanation is offered. We are also indebted to Kelly for the grouping of "cases characterized clinically by marked ascites, with little or no edema of the legs, cases in which the diagnosis of cirrhosis of the liver is usually made, and which at the necropsy reveal chronic obliterative pericarditis and certain morbid changes in other tissues and organs, notably pleuritis, peritonitis, perihepatitis, nutmeg liver, red atrophy of the liver, cirrhosis of the liver, and so forth," under the single heading of multiple serositis. As Lamb has said, the essential point to be remembered in diagnosis is the multiple lesions of the serous membrane, the relative predominance of peritonitis, pericarditis, perihepatitis, or pleuritis being of less diagnostic significance. The diagnosis should always be considered in cases of marked ascites of long duration, in which there have been many tapplings, and frequent stationary periods. Possibly there is such "remission" in Case 2 at the present time.

A search of the Mayo Clinic files revealed a group of twenty-four cases in which the diagnosis of polyserositis had been made.*

* Since these data were compiled another patient with polyserositis has registered at the Clinic. This patient is a school boy, aged seventeen, whose illness began two years ago with pain in the region of the ensiform cartilage, accentuated by exercise. Within a week low-grade fever and night sweats developed. Within a month it was necessary to aspirate the right pleural cavity. Within two months definite ascites was present, and within four months pericardial tapping was necessary. After about fifteen months treatment with ammonium chlorid and merbaphen was instituted and continued with marked success for about six months; tapping was not necessary during this period. Finally its effectiveness diminished, and it was discontinued entirely because of marked reactions. The right pleural cavity

The chronicity of the condition and the fact that it is not incompatible with fairly long life is shown by the fact that only one case came to necropsy. In seventeen cases of the group there was definite evidence of involvement of the pericardium; the pleura was affected in nineteen and ascites was found in all. In fourteen of the cases all the serous cavities were affected. Auricular fibrillation was encountered in four cases, in three of which definite signs of adherent pericardium were demonstrated. In most of the cases the abdomen had been tapped a number of times either at the Clinic or elsewhere, in some as many as thirty-five times. In one case a Talma-Morison operation had been performed, with some benefit.

The records were searched carefully for any facts that might have bearing on the etiology of the disease. Three of the patients had had rheumatic fever. The possibility of a tuberculous

was explored shortly after the onset of the illness and residual empyema resulted. At the time of admission abdominal paracentesis was necessary about every five days, five liters of fluid being the average amount withdrawn. Careful study of the fluid had been made without finding evidence of tuberculosis, and guinea-pig inoculations and tuberculin tests had been repeatedly negative.

General examination disclosed marked dyspnea, the thorax being almost completely immobilized, and the accessory muscles of respiration brought into play at every breath. There were signs of thickened pleura at the base of both lungs, and a small empyema cavity on the right. The heart was enlarged, the left border reaching 2 cm. beyond the nipple line. A questionable Broadbent's sign was present. The abdomen, which was heavily marked with lineae albicantes and puncture scars, was partly filled with fluid; the liver was palpable 6 cm. below the costal margin as a hard, smooth mass. The lower extremities and back were moderately edematous and cyanosed. Urinalysis and blood Wassermann tests were negative. Examination of the blood showed the hemoglobin to be 82 per cent; erythrocytes numbered 4,120,000, and leukocytes 12,500. Phenolsulphonephthalein excretion and blood urea were within normal limits. The bromsulphthalein test of hepatic function showed dye retention, graded 1. Roentgenograms of the chest revealed markedly increased density of the lower lobes of both lungs and thickened pleura; there was questionable evidence of fluid on the right side.

The problem of treatment in this case is difficult. Diuretics have apparently lost their efficacy, and the patient is depending on frequent abdominal paracentesis. During the entire illness the right side of the chest has been tapped five times, the left side fifteen times, the pericardium three times, and the abdomen about ninety times. Cardiolysis is being carefully considered, as it is apparent that only radical surgical measures offer any hope.

basis is indicated, since ten of the patients had had pleurisy with effusion prior to the onset of the illness. Nevertheless, the presence of tuberculosis could not be established definitely in any case in this series. The fairly constant hepatic involvement, with capsular cirrhosis, is shown by the fact that in eight cases of the series in which tests of hepatic function were carried out there was a varying degree of dye retention.

Because of the long duration of the disease, because patients survive many tapings (Rumpf's patient was tapped 301 times), and because of the stationary periods which frequently occur these cases seem to offer a particularly good field for treatment with the newer diuretics. Digitalis, caffeine and its derivatives, or calomel have not been particularly successful. Ammonium chlorid alone was effective in two cases in my series; merbaphen when given without other treatment in two cases did not produce diuresis. In five cases, however, these two remedies were combined, with excellent results; diuresis was marked and ascites was reduced rapidly. A summary of results is shown in Figure 235. It is evident "medical tapping" should be tried in cases diagnosed polyserositis before paracentesis is resorted to. The permanence of the result is not always all that could be desired, and it is usually necessary for the patient to remain on a diet which is low in salt and water content; in other cases occasional brief courses of diuretics combined with merbaphen will control the ascites.

The marked success attending "medical tapping" in the management of ascites due to portal cirrhosis has encouraged clinicians to believe that a symptomatic "cure" is occasionally obtained. Such "cures" unfortunately are not frequent, and only rarely are they permanent. It seems well established that in many cases ascites recurs much more slowly after treatment by merbaphen than after paracentesis, and in a few cases it has been relieved entirely, the serous cavities remaining "dry" over long periods. This may be explained by the development of collateral circulation or by diets poor in salts and water which the patients are advised to follow. These therapeutic successes led to attempts to treat advanced cases of portal

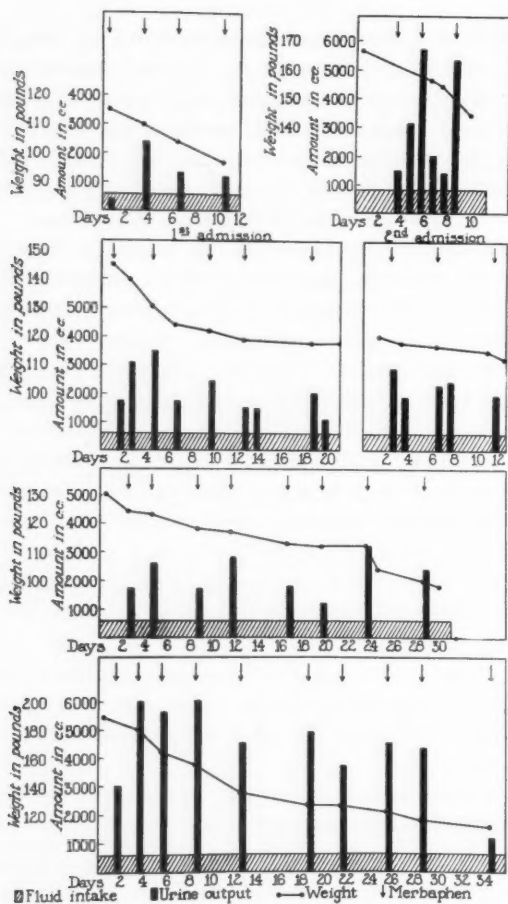


Fig. 235.—Schematic chart of the results of diuretic treatment in five cases of multiple serositis. All patients were given ammonium chlorid in doses of from 6 to 9 gm. daily and were on diets of constant salt and water content. The administration of merbaphen is recorded on the chart by arrows. The shaded areas represent the fluid intake exclusive of the water contained in the diet (800 c.c.). The urine output is recorded only on days when a significant diuresis was obtained; on the days not specifically recorded the urine output averaged 600 c.c.

cirrhosis. As might have been predicted, the results obtained in this group have been unsatisfactory, and have served to show the limitations of the methods employed. In order to make a proper selection of cases for treatment the natural course of the disease must be constantly borne in mind. Case 3 represents partial failure of treatment and illustrates some of the problems encountered in advanced portal cirrhosis.

Case 3.—A fireman aged fifty-seven came to the Mayo Clinic in October, 1927. He had had pneumonia in 1922, but otherwise had enjoyed good health up to the onset of his present illness. There was a history of moderate alcoholism of long duration. The family and marital histories were negative. The illness had begun in 1926 with epigastric distress, noted immediately after meals, with flatulence and belching; a cathartic was said to relieve these symptoms considerably. A short time after the epigastric distress was first noticed the abdomen began to enlarge, and continued to enlarge slowly and progressively for several months. Recently the patient had been short of breath and unable to move about with comfort. Two months prior to his admission to the Clinic he had suffered greatly from vomiting and nausea and had lost strength rapidly.

On physical examination the patient was strikingly emaciated and there was a definite subicteric tint to the sclerotics. The teeth had all been extracted and a double plate was worn; the tonsils were slightly infected. Examination of the thorax was negative except for elevation of the diaphragm and slight increase in the cardiac diameters. The abdomen was distended with fluid and a moderate collateral venous circulation was noted on the anterior abdominal wall. Bilateral direct inguinal hernia and moderate benign enlargement of the prostate were present; moderate peripheral arteriosclerosis was also noted. There was no edema of the ankles or face. The systolic blood pressure was 150 and the diastolic 90. Urinalysis, blood count, and blood Wassermann test were negative. The phenolsulphonephthalein return was 60 per cent in two hours and the blood urea was 18 mg. for each 100 c.c. Roentgenograms of the chest showed a slightly thickened pleura at both lung bases with marked elevation of the diaphragm. Tests of hepatic function showed dye retention graded 3. The blood serum gave a direct van den Bergh reaction, and the serum bilirubin varied from 1.5 to 3.5 mg. for each 100 c.c. Electrocardiograms showed sinus rhythm, left ventricular preponderance, and inversion of the P and T waves in Derivation III. The total blood volume was 87 c.c. for each kilogram of body weight.

A diagnosis of portal cirrhosis, probably on an alcoholic basis, was made and treatment instituted, the patient being given ammonium nitrate in doses of 6 gm. daily, and merbaphen in doses of 1 to 2 c.c. intravenously every fourth day. The response to treatment was slight, the maximal twenty-four-hour output of urine being 2,250 c.c. The fluid balance is shown in Figure 236. The patient continued to lose weight, however, and the ascites decreased somewhat in amount. He vomited at intervals and it was difficult to continue

oral medication. Euphyllin in doses of 0.2 gm. three times daily was added to the treatment, but did not effect striking results. Throughout the two weeks when the patient was under observation he appeared to be losing ground, and was consequently advised to return to his home. The ascites was moderately diminished at the time of his dismissal, having been reduced sufficiently

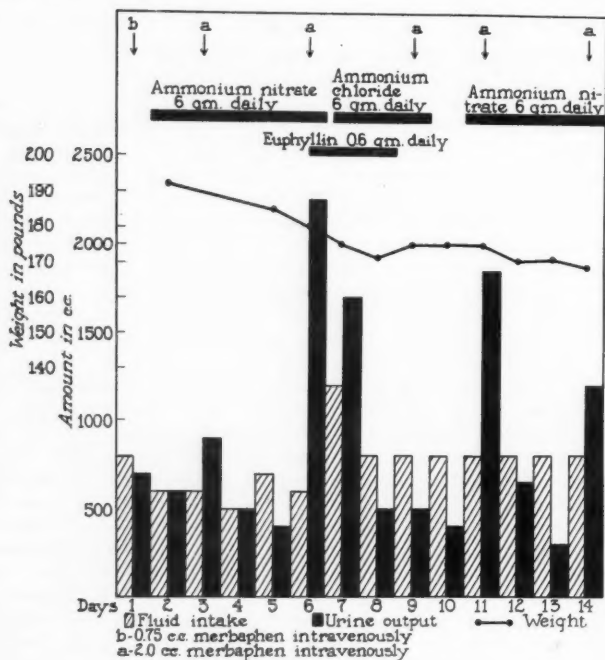


Fig. 236.—The result of diuretic treatment in an advanced case of portal cirrhosis. The fluid intake is recorded as that taken in excess of the water content of the diet (800 c.c.).

to relieve dyspnea and make him more comfortable. Masses were not found in the abdomen at any time, and the liver edge was just felt at the costal margin at the time of dismissal. The slight latent jaundice, as shown by serum bilirubin studies, persisted throughout the patient's stay in the hospital.

There are a number of clinical manifestations that have been regarded of grave prognostic significance in ascitic cirrhosis. Among these may be mentioned progressive cachexia, severe

and frequent gastro-intestinal upsets, mental disturbances, recurrent hematemesis or melena, and, in some instances, jaundice. The latter condition may be among the earliest signs of cirrhosis, or it may constitute part of the terminal picture, along with coma or other evidences of so-called hepatic toxemia. A case presenting one or more of the foregoing complications must be regarded as unsuitable for active medical treatment; I have seldom found it possible to accomplish anything with diuretics in such cases, and there has been some reason to believe that efforts to relieve the patient may have accelerated the progress of the disease. A progressive decline in the effectiveness of diuretic remedies has been a prominent feature in some of the cases under observation, and in many instances it has been possible partially to correlate the clinical evidence of the patient's decline with the gradually diminishing therapeutic results. Such a case has been cited recently by Rowntree. This correlation has led us to believe that a poor response to diuretics has almost as much prognostic significance as the clinical data mentioned.

There are not many absolute contraindications to a trial of treatment, although in many cases it would seem inadvisable. Jaundice seems to interfere at times, particularly when the ascites is of long duration and the jaundice a recent development, as is illustrated in Case 3. Slight elevation of blood urea and failure to concentrate urine are often among the earliest signs of mild renal insufficiency, which is an almost insurmountable barrier to therapeutic success. The ammonium salts dissociate in the body into ammonium and acid radicals, the former being converted to urea and the latter combining with fixed base. If renal elimination of these radicals is impaired, there is a rapid accumulation of urea in the blood together with marked decrease in the carbon dioxid combining power of the plasma. The possible toxic action of mercury on a previously diseased and inefficient kidney is obviously to be avoided if possible.

Untoward reactions to treatment may also constitute an effective check to the relief of ascites by medical means. Of these reactions the most significant are general decline in the

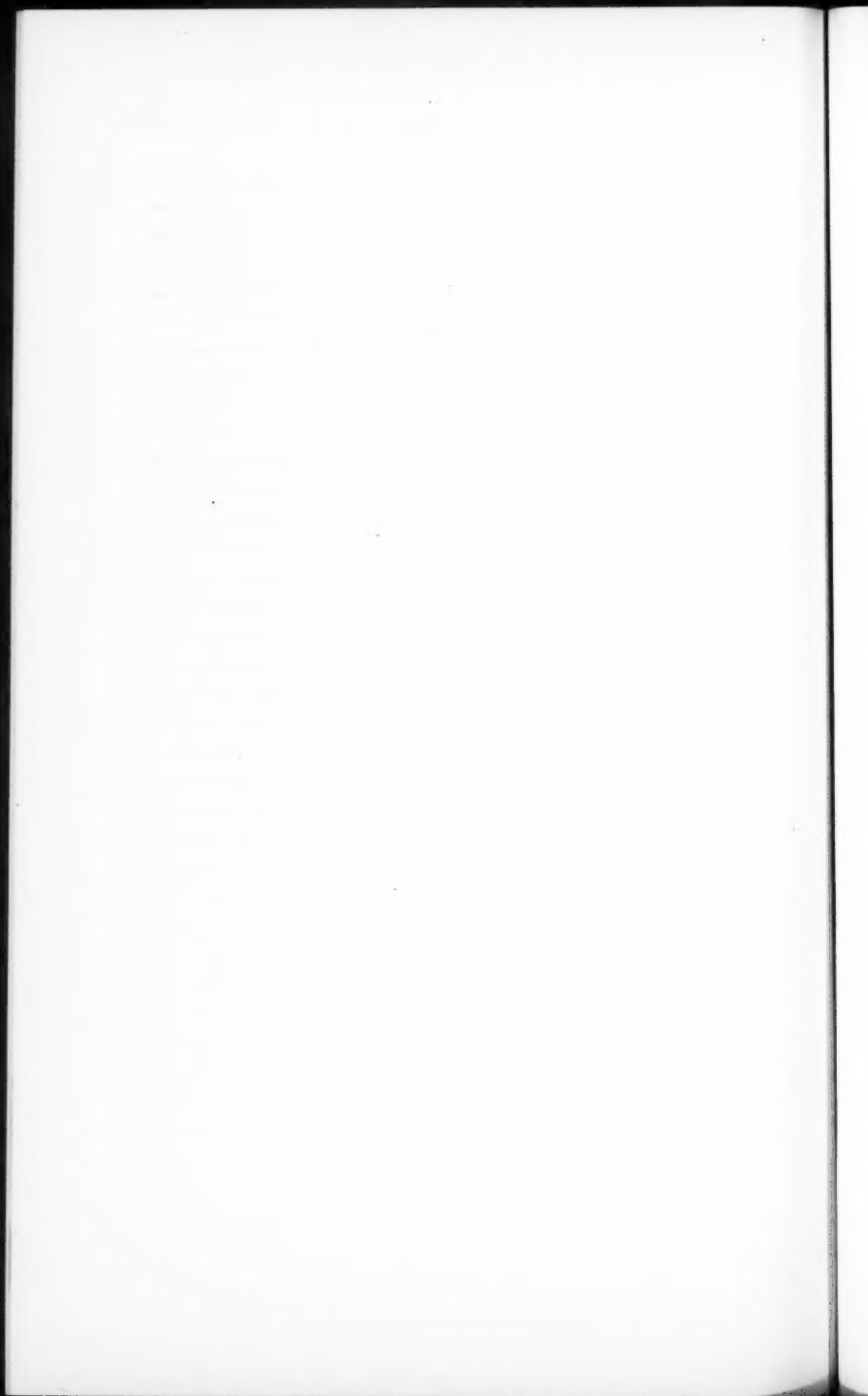
patient's physical strength and the development of peculiar lassitude. These symptoms may be the earliest signs of impending diaster. Other reactions encountered in the treatment by ammonium salts and merbaphen include stomatitis, diarrhea, and toxic eruptions of the skin with purpuric manifestations; these are incidental to the mercury content of merbaphen. The ammonium salts may cause nausea and vomiting, but otherwise seem harmless except in the presence of renal insufficiency and in certain cases in which obscure types of psychosis develop, suggesting ammonium intoxication. The "hepatic toxemias" and their relation to treatment have been discussed previously by Weir and the author; it is probable that these toxemias occur independently in advanced cases and are not precipitated by treatment.

Tests of hepatic function are of rather doubtful value in the selection of cases for treatment. While patients with high grades of dye retention are often resistant to treatment and the prognosis in these cases is probably poor, there are so many exceptions that no general rule can be formulated. The exact cause of dye retention in portal cirrhosis is not entirely clear, although McIndoe's work indicates that it may be due principally to reduction in the total amount of blood reaching the hepatic parenchyma. McIndoe has shown that in advanced portal cirrhosis practically 100 per cent of the venous blood from the intestines must be diverted through collateral channels, the blood supply of the hepatic tissue being derived almost exclusively from the hepatic artery which normally furnishes less than half of the total hepatic circulation. There is probably not sufficient reduction in the total number of hepatic cells to explain the failure of the liver to remove dye from the blood stream. Rowntree and his associates found that practically the normal amount of phenoltetrachlorophthalein was excreted in the stools of twenty-four hours, thus indicating that the liver was capable of removing the dye from circulation, although not at a normal rate.

In conclusion, it may be said that a consideration of the patient's general condition, the duration of the ascites, the

state of the cardiovascular and renal apparatus, and a study of the serum bilirubin to detect latent jaundice are quite as important as the dye tests when the advisability of medical treatment in ascitic cirrhosis is in question. In borderline cases a cautious therapeutic trial, with the patient under observation in the hospital, will settle the question; the subjective improvement of the patient after a satisfactory diuretic response will stamp the case as a favorable one for continued treatment, while partial or total failure of the treatment is often indicative of a grave prognosis.

It is perhaps unnecessary to discuss our ignorance of the manner in which many pathologic changes give rise to ascites. The accumulation of fluid in the peritoneal and pleural cavities from benign solid tumors of the ovary, the spontaneous remissions observed in portal cirrhosis and polyserositis, and the effusions in serous cavities accompanying chronic nephrosis are still totally unexplained. Our explanations of ascites in chronic heart failure and portal cirrhosis do not satisfy many critical minds. Our ignorance of the various mechanisms by which ascites may be produced is only exceeded by our lack of knowledge of how such diuretics as merbaphen act to relieve the condition. The diuretic treatment is, however, productive of extraordinarily good symptomatic effects in selected cases, and may give, as has been shown, valuable clues as to diagnosis, prognosis, and proper treatment.



HYPERTENSION AND APPENDICITIS IN EIGHT MEMBERS OF ONE FAMILY

WALTER C. ALVAREZ

It is unfortunate that the consulting physician in a large city or clinic must see almost all of his patients as individuals apart from their background of heredity. To be sure, he ordinarily asks a few questions about the family history, but usually all he gets is a vague idea as to the cause of death of the father and mother; seldom does he learn all he should about the family tendencies to disease, and the way in which the particular body before him is likely to break down under strain.

In the early days of my practice when I visited some of my patients in their homes I found myself inclined at times to give a more hopeful and, as events proved, a more correct prognosis in regard to a certain illness because I had seen other members of the family triumphing over it with ease. At other times a knowledge of family weaknesses caused me to recognize mild hypothyroidism, pernicious anemia, or myocardial failure earlier than I might otherwise have done.

One of the evil consequences of our present mode of practice is the tendency to look on the complaints of patients as isolated diseases that can be cured by a short course of medication and the removal of teeth and tonsils. If we knew more about the natural history of disease we would more often see that the "neuritis" we are treating represents but one episode in the course of a smouldering infection which began in childhood and which will continue to flare up at intervals until, perhaps in his late sixties, the patient will die with terminal bronchopneumonia or pyelonephritis. The frequent colds of youth, the "toxic spells," the sinusitis, wry neck, lumbago, sciatica, appendicitis, cholecystitis, duodenal ulcer, and prostatitis which appeared at intervals during a long life were all parts of one disease. Similarly,

albuminuria, frequent urination, a large irritable heart, and cold, bluish hands in youth are part of the picture of hypertension which may show itself later in a certain amount of hypochondriasis, some dyspnea on exertion, morning headache, and dizziness. Many of the conditions that now puzzle the pediatrician must, I feel sure, be early signs of "diatheses" which later are going to manifest themselves in forms more easily labeled.

When we see a patient departing well and happy after a course of treatment we naturally get the idea that we have cured him and that the therapeutic measure used will work just as well in the next similar case. Unfortunately for us and the progress of medical science, when the next attack of the disease or, let us say, the next episode appears, the patient does not always come back, and we remain in our comfortable state of ignorance. Perhaps the invalid has moved away, or he wants to try a new physician, or, the symptoms having changed, he decides that he must go to another type of specialist. To show what I mean: In 1913 I saw a woman with severe headache which was so much improved after the removal of some infected teeth that I thought I had cured her. A year later, however, I met a laryngologist who told me that he had seen her with the same headache and a large lymph node at the ramus of the jaw. He had cured her by removing her tonsils. Later a gynecologist told me that he had cured her by removing a fibroid tumor of the uterus, and still later a psychotherapist boasted that he had succeeded where the rest of us had failed. The patient slumped again, however, and was next cured by an oculist. Later an aurist took charge on account of deafness in one ear and roaring noises. Finally, when nine years after the onset of her illness she began to vomit, she returned to me, and I then had no difficulty in recognizing the symptoms of brain tumor. Biopsy of a lymph node in the neck showed the lesion to be a slow-growing endothelioma, and at last all the curious symptoms of the preceding years could be fitted into one picture.

For years I have felt with Sir James Mackenzie that we should pause in our research work long enough to see that there

is much that we should learn about the life-history of disease from the moment when it attacks the child until it stops the beat of the old man's heart. We cannot learn all that we need to know by questioning old men and women, because diagnosis sixty years ago was not what it is today, and even the most intelligent persons in middle life cannot remember much about the illnesses of their youth. That much interesting and useful information can be obtained, however, by working backward in this way has recently been shown by Willius in his study of the duration of life of patients with acute articular rheumatism.

Unfortunately, our lives are not much longer than those of our patients, and much of the information that is needed will have to be gathered later by our medical heirs and assigns. They alone can finish the records that we are now making on children and young persons. Much can be done now, however, if we will only study our patients more attentively, with our eyes open to discern the protean manifestations of disease as it progresses in individuals and in families. The fact that in one family hypertension, heart disease, and nephritis often appear to be interchangeable seems to me to throw light on the nature of hypertension, and the fact that in another family pernicious anemia, leukemia, and a tendency to diarrhea and mild anemia seem to be interchangeable throws light on the relationships of these diseases.

During the last fifty years the medical profession has been so impressed with the advances in knowledge that have come from the use of laboratory instruments that some of the older methods of studying the manifestations of disease have been neglected. We are proud of our knowledge of the bacteriology and the chemistry of disease; we are not yet sufficiently ashamed of our inability to answer such simple questions as: How many normal persons are constipated? or How many normal persons have focal infections? There is a tremendous amount of work that can be done by anyone with a questioning mind who will start a notebook and keep his eyes and ears open. He does not have to become a bacteriologist or a biochemist to do interesting and valuable research work.

For years the guinea-pig has been regarded as a guinea-pig, just as standardized in its reaction to disease-producing organisms as an agar slant, but recently workers in several lands have come to see that the resistance of the guinea-pig is a decided variable, and that particularly in studies of chronic disease, such as tuberculosis, they must know, when they inoculate an animal, that it belongs to a certain pure strain, the members of which have been found to respond to infection in a certain way.

During the last few years a number of gastro-enterologists have come more and more to suspect that certain persons are strongly predisposed to the formation of peptic ulcer. The surgeon cuts one out, and within a few months the patient is back with another and even larger defect in the mucous membrane of stomach or jejunum. Mann experiments on animals and learns much about the factors involved in the production of ulcer, but his problem is made difficult by the fact that the dog with which he is working has none of the family predisposition which may perhaps play so large a part in producing ulcers in men and women.

With these thoughts in mind I wish now to present a somewhat unusual type of clinic, but one which I hope will be seen more and more frequently as time goes on. Instead of presenting the records of individuals I am telling the stories of eight persons: a mother, a father, two sisters of the father, and four children (all but one of whom I have known as physician and friend for fourteen or fifteen years). I present these records not because they are particularly remarkable or because they are unusually complete, but because I wish to stimulate more interest in this way of studying disease.

W. F., Sr., a railroad engineer and the father of the four children whose histories are reported here, died several years before I met the family. He had had chorea in childhood, and later, after an injury to his knees, he suffered with rheumatism and for a time was in a cast. At the age of thirty-four he was seized with abdominal cramps, but kept at his work until peritonitis pulled him down. He died a few hours after an operation. The cause of death was supposed to be intestinal obstruction, but my subsequent experience with his four children makes me suspect that there was an unrecognized appendicitis.

K. F., the mother of the four children, was first seen by me in 1912, when she was forty-two. She complained of headaches and flushing. An aunt had suffered with hypertension and hemorrhages. As a girl the patient flushed badly. Before her marriage she had a long illness diagnosed as malaria. She had no difficulty carrying the first three children, but was miserable much of the time during the last pregnancy. She had always had a tendency to diarrhea when nervous. When first seen by me all her troubles could be attributed to a blood pressure of 280 and 145. In June, 1914 bleeding began, apparently from the stomach, and in a few hours the hemoglobin dropped to 15 per cent and the systolic blood pressure to 125. After a transfusion she slowly recovered.

Röntgenologic examination showed an atonic stomach with an area near the greater curvature where the markings of the mucous membrane were irregular. No definite ulceration could be seen and there was no history suggesting ulcer. The aorta was widely dilated. For a month there was fever and some diarrhea, but by August, 1914 she was better and the blood pressure was 195 and 115. A week later she was having severe flushes and anginoid pain, and the blood pressure was 210 and 110.

In January, 1915 the patient was waking at 3.00 a.m. with headache and pains in the legs; there was some regurgitation and nausea and a feeling of being cold under the skin. Menstruation was irregular. The blood pressure was 248 and 114. She went through the year fairly well.

In January, 1916 menstruation stopped. She was then getting up four times at night to urinate. She again began to have pain back of the ears in the area supplied by branches of the vagus nerve. This pain was severe during the hemorrhage and it returned at frequent intervals. In December she was feeling well in spite of the fact that the blood pressure was 260 and 120. In May, 1917 she still was doing well except for weakness and pain in the knees. The blood pressure was 230 and 125. In July headache returned and in a month symptoms of intracerebral pressure became so alarming and so uncontrollable that a liter of blood was withdrawn from a vein. The reaction was the reverse of what we had hoped for: she suffered greatly from nausea and a feeling of impending death and neither she nor I cared ever to repeat the experience. The systolic pressure dropped immediately to 120, it remained there for several days, and then rapidly went back to 280. For months afterward she was weak and miserable.

In July, 1918 she reported that symptoms had come only in spells; digestion was good, there was slight dyspnea, and occasional pain back of the ears. The blood pressure was 230 and 160. During the next year there were several attacks of headache best relieved by theobromin sodiosalicylate. In July there was a severe hemorrhage following the removal of a tooth, and this time the bleeding seemed to bring relief in spite of the fact that within two weeks the blood pressure was back to 258 and 148. In 1920 there was some vomiting and in 1921 more hemorrhage from the stomach, but, on the whole, she did fairly well and was able to do all the work for her family. She looked strong and ruddy. In May, 1922 I heard that she had died from diphtheria.

J. F. C., the father's sister, is a frail little woman, aged fifty-three, who remains sweet and sensible in spite of the fact that for most of her life she

has been an invalid with weak lungs and weak digestion. Between the ages of sixteen and twenty-eight she went through four attacks of pneumonia. Her first baby died with a patent foramen ovale. Her second pregnancy was so stormy with asthma, bronchitis, and vomiting that it had to be interrupted. Two years later she was in bed three months with "grip" and a dilated heart, and after that she had to take a rest cure for six months.

I saw the patient first in 1912 when she was complaining of nervousness, weakness, a stinging feeling in the left side of the tongue, nausea, backache, pain in the stomach, and depression. She was much depressed for a day or two before each menstrual period. Between 1917 and 1922 she suffered with repeated attacks of bronchitis accompanied by asthma. So far as she knows no other members of the family are troubled with asthma. In 1917 she was bothered with hemorrhoids and flatulence. The blood pressure was 145 and 90; at times it dropped to normal, but in 1919 it was 155 and 90.

In 1919 urination was sometimes painful and the eyelids were puffy. The urine was normal. The heart was then slightly enlarged, there were adhesions to the diaphragm on both sides, both kidneys were floating, the cecum was large and tender, the left ovary was tender, and the uterus was somewhat enlarged with a bleeding polyp in the cervix. In November, 1919 the cervix was removed and the ulceration there found to be benign. The abdomen was explored and a "chronic appendix" was removed. There was no improvement in health following these procedures.

In 1920 the patient suffered severe abdominal cramps and a small stone in the left ureter was removed through the bladder. In October, 1920 there was another violent attack of cramps, vomiting, and diarrhea due either to enteritis or another stone. Following this illness she was tired, depressed, and weak; she complained of some arthritis and mucous colitis and finally had to take a seven months' rest cure in a sanatorium.

In 1921, at the age of forty-seven, menstruation stopped and there were hot flashes and backache. Strange to say, the blood pressure returned to normal and the asthma practically disappeared. Although the patient is still asthenic, and suffers occasionally from sciatica, her health is now better than it has been for years. She is probably correct in ascribing this improved health to the fact that at last, now that her nephews and nieces are all self-supporting, she can afford a good maid.

F. F., the father's sister, is a well-developed, highly nervous, and asthenic woman, aged sixty-seven. All her life she has been subject to bilious spells. She thinks she has had typhoid fever twice. About 1900 she suffered her first severe attack of pain in the region of the gallbladder, and for years afterward the bilious spells were so bad that she had to spend three or four days of every month in bed.

In 1917, when I first saw the patient, she had most of the signs and symptoms which we now recognize as being those of cholecystitis. The region of the gallbladder was tender, the tonsils were very bad, the aortic arch was definitely widened, and the blood pressure was 148 and 95. In spite of the fact that she had never married or borne children the uterus was markedly prolapsed.

Roentgenologic examination on several occasions showed a markedly

narrowed, rigid pars pylorica, strongly suggesting the presence of carcinoma. After six hours the stomach contained considerable residue. At operation the gallbladder was thought to be normal and was not removed. The lower third of the stomach was so rigid that it was removed, the surgeon fearing that he was dealing with a linitis type of carcinoma. Microscopic examination, however, showed only some hypertrophy of muscle and connective tissue. After a month of almost constant nausea the patient recovered and for several years her stomach gave her little trouble.

In May, 1918 the patient returned, complaining of fatigue, insomnia, and severe arthritis of the neck similar to what she had had at the age of eight. At intervals in the past she had also suffered from lumbago. In July, 1918 she complained that her tongue felt queer. In September, 1921 arthritis of the spine was the principal source of discomfort. In August, 1922 the stomach trouble returned, with spells of vomiting. In September she had an attack of acute cholecystitis. I saw her at intervals up to 1925 with typical attacks of cholecystitis. Roentgenologic examination showed a normal stomach except for the resection. In July, 1925 hysterectomy was performed to relieve the prolapse, and since then the patient has been so much better that she is going to try and live out her days without cholecystectomy.

M. F., a daughter of W. F. and K. F., is a stout, red-cheeked young woman of twenty-five. I saw her first in 1914 with an "exploded appendix." Drainage of the lower part of the peritoneal cavity was secured, and after several stormy weeks she recovered. During convalescence she was troubled with cystitis. In August, 1914 she had an attack of herpes. In 1915 she began to menstruate. The flow was scanty; it came twice a month and caused much pain. In December, 1916 there were further signs that the ovarian secretion was not sufficient; menstruation was still troublesome and the blood pressure was 130 and 85, too high for a girl of fourteen. In May, 1917 she complained of flushing badly like her mother and sister. She felt cold all the time, although the skin was full of blood and warm to the touch. She was beginning to get fat. She had been vomiting, often right after meals, and at times she was hysterical and hard to control.

In August, 1918 there was an acute attack of vomiting, chills, and fever, and a few days later acute trigonitis was found with a number of small ulcers in the mucous membrane. This did not yield well to treatment, and for the next two months the patient complained of nausea, pain after eating, vomiting, flatulence, and constant fatigue. In September, 1918 roentgenologic examination showed the heart a little large and the stomach and colon normal. Renal function was apparently normal, but there was still marked trigonitis. In October, 1918 she reported that an acute attack of influenza had cured the bladder and stomach trouble!

In November, 1922 the patient vomited some blood and suffered with severe nosebleeds, which, with the stoppage of menstruation, suggested a vicarious escape of blood. She felt doxy and could not study. She had not menstruated for eight months. The stomach was behaving fairly well and the bowels moved normally. She still was hysterical at times. The blood pressure was 135 and 85. The uterus was retroverted and bound down.

December 26 operation was performed, with the hope of saving some

ovarian function and also of improving conditions in the bladder. The omentum was found plastered firmly over the pelvic organs, the bladder was fastened high on the uterus, and the fundus of that organ was fastened to the rectum. The ovaries were covered with omentum and bowel. Both ovaries were small and the right one was practically destroyed. Conditions in the pelvis were restored as nearly as possible to normal and raw surfaces were covered with peritoneum. There were adhesions about the duodenum and the gallbladder was full of stones, showing that I had probably done the girl an injustice in ascribing most of the vomiting to hysteria. She doubtless acted hysterically at times, but, like so many of the neurotic and the feebly inhibited, she had an organic peg on which to hang her symptoms.



Fig. 237.—The narrowed duodenum of M. F.

Shortly after the operation she began to vomit within an hour after every meal. There was pain in the region of the gallbladder and the urinary bladder began to bother her again. She became very dizzy. In February, 1923 she reported that the urinary bladder was better, but she continued to have repeated attacks of cholecystitis. She said she ate little, vomited that, and gained in weight! With her short stature a weight of 163 pounds was too much.

March 2, 1923 the gallbladder, full of stones, was removed. The pelvis was in good condition except that the left ovary had enlarged to four times normal size. She was not out of the hospital before she again was seized with severe headache, dizziness, flatulence, and vomiting. Her weight was 154 pounds and the blood pressure 134 and 86. March 26, 1923 she had an attack of gallbladder colic. Roentgenoscopic examination showed marked

spasm of the pars pylorica. The second portion of the duodenum was a narrow tube 7 mm. in diameter and 9 or 10 cm. long through which the barium meal could with difficulty be forced (Fig. 237).

The patient went from bad to worse, and April 16, 1923 gastro-enterostomy was performed. The duodenum was obstructed by adhesions that bound it to the liver. Convalescence was stormy and she continued at intervals to vomit so much that on February 11, 1924 she had to be operated on again. The pars pylorica was then separated from the body of the stomach with the hope of interrupting the course of reverse waves originating in the irritable duodenal region. This hope was justified, and at last she was able to return to her occupation as a student nurse. March 7 she reported herself cured. I hear that she still has occasional attacks of vomiting, but she has been able to keep at her work. She now shows a typical hypopituitary type of obesity with most of the fat below the waist. She sometimes goes a year without menstruating and then flows to excess.

W. F. is a well-developed, well-nourished young man of thirty-one. As a child he suffered from severe intestinal upsets. In 1914 his sister, M. F., had barely recovered from appendicitis when I was called to see him in an attack of the same disease. He was promptly operated on and convalescence was uneventful. In August, 1915, when he was nineteen, he consulted me again because of nosebleeds and cough. He had always been very thin; at the age of fifteen he weighed only 69 pounds. He had been troubled with nosebleed for years; it came with extra exertion or in hot weather. Otherwise he showed no signs of being a bleeder. His father had suffered in the same way and later his sister, M. F., had frequent nosebleeds. His digestion was easily upset, his wind was fair. He did not rise at night to urinate.

In 1915 the patient was 5 feet 9 inches tall and weighed 111 pounds. The lungs were clear and the heart overacting. The teeth were bad. Examination of the urine showed a large amount of albumin. By September 5, with rest and a change in diet, he had gained 5 pounds, and the albumin had disappeared from the urine. Ten days later he had gained 5 more pounds, there was no albumin, and the systolic blood pressure was 148. In December he went through an attack of bronchitis. There was no sign of tuberculosis; the urine was normal and the blood pressure 155 and 110; the second aortic sound was markedly accentuated. In August, 1916 there was some bleeding from the nose, but otherwise he was well; the blood pressure was 148 and 90, the weight 118.5 pounds, and the urine normal. The heart was still over-acting.

In September, 1924, while the patient was in Washington, D. C., he began to have epigastric pain relieved by food and soda. Duodenal ulcer was diagnosed, and for one month he underwent treatment in a hospital. In January, 1925 he was still dieting, although he felt well. The blood pressure had dropped to 125 and 84. Roentgenologic examination showed the heart normal in size and the outlines of the stomach and cap perfectly smooth. He had gained 10 pounds and looked well. In June his weight was up to 154 pounds and he stopped taking food between meals. In December he reported himself well; he weighed 158 pounds; he had stood a high mountain trip well; he occasionally had flatulence; the heart was always overacting; the blood

pressure was 150 and 90; there was no albumin in the urine. A recent letter tells me that he is doing well and he has come safely through the anxieties incident to the birth of his first child.

J. F. is a well-built, red-cheeked, auburn-haired unmarried woman, aged thirty. I saw her first in July, 1915 with what appeared to be subacute appendicitis. She recovered from this attack and for financial reasons deferred operation until 1922, when recurrent attacks of indigestion forced her to undergo it. Examination showed the pulse to be 120, markedly influenced by respiration and excitement. A slight thrill was felt over the apex of the heart. At eighteen her blood pressure was already 150 and 85. She was much bothered by severe flushing. The circulation in the hands was poor and she was troubled even in moderately cool weather by "chilblains" on fingers and ears. She was dizzy and short of breath when she walked fast, and she often felt as if she would faint.

In December, 1916 the blood pressure was 160 and 75. Like her mother, she had occasional spells of nervousness with vomiting and diarrhea. In September, 1922 she complained of dyspnea on exertion and the blood pressure was 156 and 84. In March, 1923 she began to have anginoid pain. During the last four years she has been in fair health except for scanty and painful menstruation which has bothered her a long time.

E. F. is a large muscular man with a ruddy complexion, aged twenty-seven. I saw him first in April, 1914, when the lymph nodes near the rami of the jaw were enormously swollen on account of ulcerated teeth. I noted then an irritable heart and the markedly cyanotic hands that I have so often seen associated with hypertension in boys and young men. I saw him in September, 1918, as he was recovering from an acute attack of appendicitis. As the family finances were then in bad shape, operation unfortunately was postponed until July, 1919, when, while away from home, he had another violent attack, was operated on, and barely escaped with his life.

I regret that I have no records in regard to blood pressure in this case. Recent letters report that the patient is well, but on account of the cyanotic hands I fear that some day he will show more definitely the family tendency to hypertension.

DISCUSSION

All four children in one family had to have appendectomy, and in three the disease of the appendix was fulminant. The assumption is that they inherited a tendency to the disease from their father who died from what may well have been a "ruptured appendix." Two sisters of the father appear to have "poor materials" in the digestive tract; one has had an appendectomy, the other is suffering with cholecystitis. Poor resistance to infection is shown perhaps in the tendency of the father to chorea and of one of his sisters to pneumonia. It can perhaps be traced back to the father's father, who fought lung

trouble all his life, and possibly to the father's grandparents who died early in life. The tendency to chorea and arthritis came apparently from the father's mother, who for years was a sufferer from valvular heart disease and sciatica. From the father's side there came also a markedly asthenic type of nervous system.

From the mother's side there came a strong tendency to hypertension which shows itself in all four children. Abnormality in the vasomotor system can be seen also in the distressing flushing of the mother and both daughters and in the cold bluish hands of one daughter and one son. Two of the children have markedly irritable hearts, and one, for a time, had large amounts of albumin in the urine.

The high incidence of hypertension in the four children suggests that they may have inherited the tendency also from the father's side. I do not know what the father's blood pressure was, but it is suggestive that a sister shows a tendency to hypertension, and an uncle died early with a stroke.

In many families in which there is hypertension I have noticed a marked tendency of the disease to show itself in childhood and youth, as it did in the case of W. F., and then to leave the victim practically free from symptoms until he is past middle age. In another family with a marked hereditary tendency to hypertension I saw a boy of fourteen with 0.4 per cent albumin in the urine and some symptoms of ulcer. Roentgenologic examination of the stomach showed nothing and with a few weeks of rest in bed all the symptoms disappeared. That was seventeen years ago, and the boy has grown into a strong man with as yet no sign or symptom of nephritis.

Several years ago while studying the blood pressure of several hundred high school boys and girls I was struck by the fact that many of those with hypertension were markedly undernourished, as was W. F. My impression was that this was an associated symptom and not a cause of the high blood pressure.

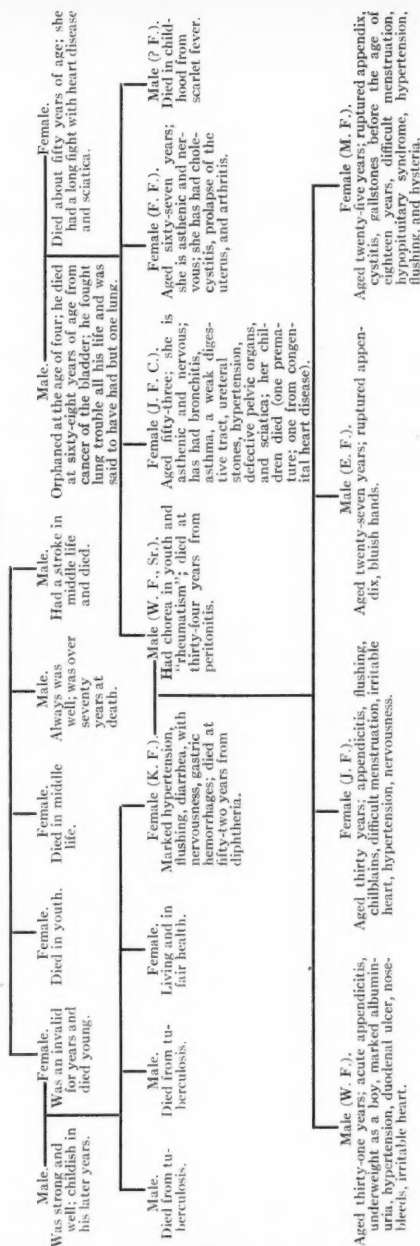
The pain back of the ears in the area supplied by branches of the vagus is of great interest. I have seen it in a few cases beside that of K. F. It was particularly severe during the hemorrhage from the stomach. Those physicians who are in-

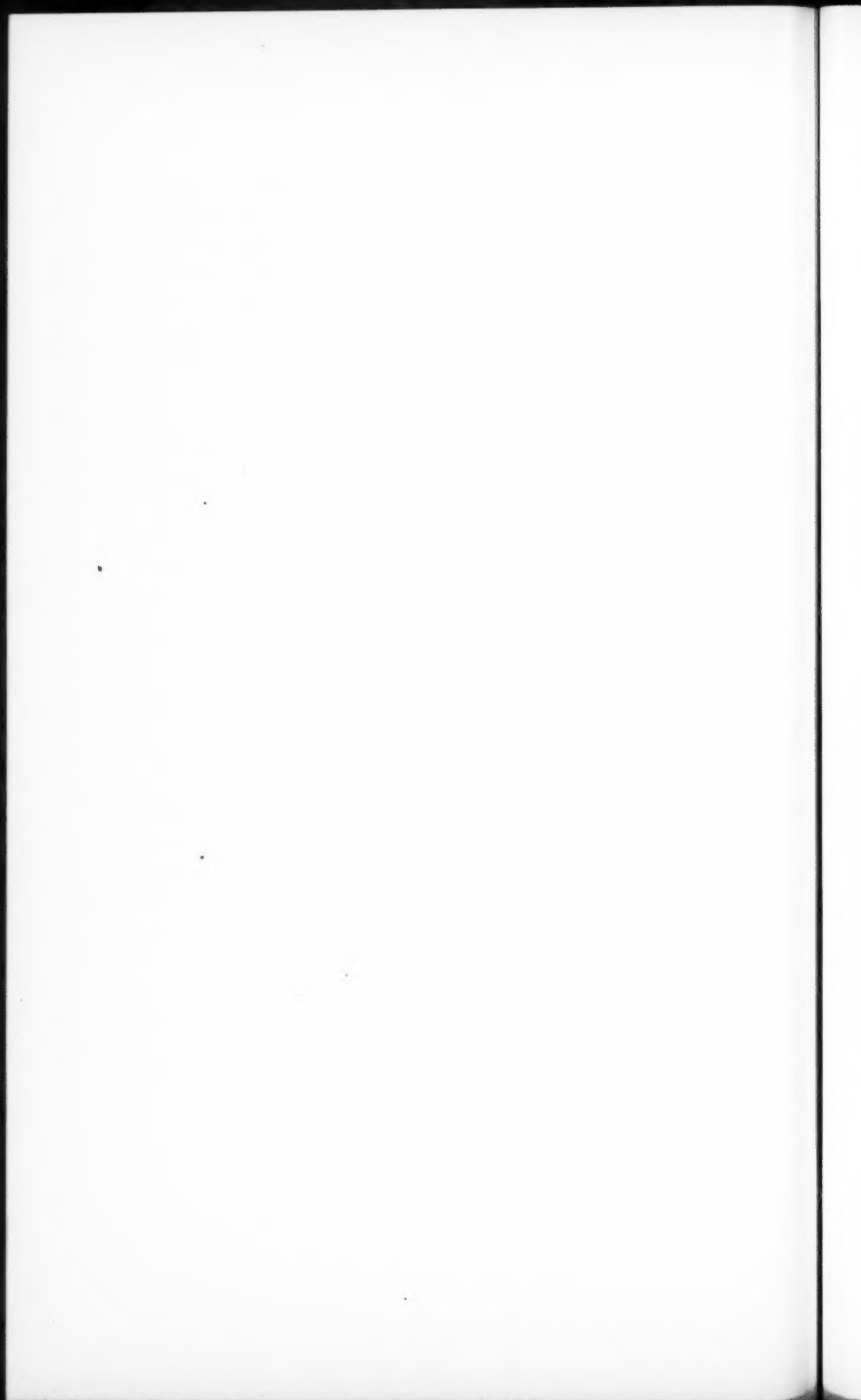
clined to bleed patients suffering from marked hypertension will find little encouragement in the story of K. F. She felt that the treatment was worse than the disease, and, after all her distress, the pressure promptly returned to its old level. Some may feel that the amount of blood removed was excessive, but in my experience the removal of smaller amounts has no effect at all.

I have often been impressed by the way in which women like K. F. can live for years with blood pressure near 300 mm. of mercury. I think they stand such pressure better than men. Interesting also is the fact that symptoms come in spells with intervals of fair comfort between, and that the height of the pressure does not correlate well with intensity of symptoms. The marked flushing of the face and neck is almost always seen in women who either have red hair or hair in which the red pigment is obscured by black. So far as I can remember I have yet to find a woman with such flushing who hasn't red-haired relatives.

If there is a hereditary tendency to appendicitis, as there seems often to be, the disease should become more and more common through the survival of the "unfit," that is, the thousands of young men and women who, if it had not been for the surgeon's prompt intervention, would not have lived to marry and to pass on their defect. Unfortunately, appendicitis is so wide-spread a disease that only the careful statistical analysis of a large amount of material could establish the truth or falsity of my hypothesis.

ABSTRACT OF FAMILY RECORD





CERTAIN ASPECTS OF ENDAMEBIASIS

PHILIP W. BROWN

THE identification of *Endamæba histolytica* in the stool or in pus from a discharging sinus may promptly establish the etiology of a disease or morbid process. However, the etiologic significance of the presence of the parasite is not constant and complications occur in the course of the disease. It is my purpose to illustrate in the following cases certain important considerations in these variations.

REPORT OF CASES

Case 1.—A native of Nicaragua aged thirty-six had complained for twenty years of spells of diarrhea, often associated with blood and pus in the stools. *Endamæba histolytica* was found in the stools and the proctoscope showed an ulcerated rectum contracted in its lower 18 cm. Roentgenogram of the colon showed a filling defect of the rectum and dilatation above it. Medication consisted of 15 grains of emetin, coal-oil enemas, and chapparo amargoso orally. Following this the ameba persisted in the stool. A course of four doses of arsphenamin was given and after this a series of examinations of the stool was negative. The patient returned three years later. During this interval the dysentery had recurred and he had been given much bismuth, emetin, and yatren. The endameba were again found in the stool. The tubular contraction of the rectum persisted. During this sojourn local treatment was applied to the rectum and three courses of treparsol (fifteen tablets in each) were carried out. At the conclusion of this stool examinations on six days were negative and the rectal mucosa appeared much more normal, although the bowel was still contracted. The patient took two more courses of treparsol after being dismissed. Recently (September, 1927) he returned because of the presence of anal fistula. There had been no dysentery for an entire year. Stool examinations on four successive days were negative and the rectal mucosa, as well as the lumen, was in better condition than on any previous visit. During the last visit the fistula was treated successfully.

This case demonstrates two distinct problems: the rebelliousness of the parasite to treatment, and the rectal stricture that may result in a long-standing case of amebic dysentery.

Repeated courses of emetin, yatren, and bismuth seemed to bring about little more than brief remissions. In this case treparsol seemed to prove effective, for, in the examination one year after the five courses of the drug, the patient was clinically well and parasites could not be found. The long-continued amebic proctitis, aided by secondary infection, has reduced the lumen of the rectum by half. Now that the primary infection seems to be eradicated there should be no further contraction and a functionally adequate rectum remains. It is to be hoped that there will be no reinfection, as re-activation of disease in the rectum may produce enough injury to necessitate colostomy.

In my experience with stovarsol and treparsol during the last three years there seem to have been fewer recurrences than with emetin. There is always the danger of an acute reaction to the drug, as well as the possibility of neuritis following its prolonged administration. The former complication occurs in about 2 per cent of the cases, while the latter has occurred once in more than 300 cases. In this particular case seventy-five stovarsol tablets were taken in three months. The neuritis appeared with a recurrence of the dysentery. More stovarsol was administered under the supervision of the local physician and a severe grade of peripheral neuritis unfortunately resulted. In several cases observed much greater quantities of the drug have been taken in a shorter space of time without causing neuritis. Hence, the individual susceptibility must determine the complications.

Case 2.—The patient was a man aged thirty-five, a native of Croatia, who had been in the United States for seven years, living in Montana. He had suffered for four months from severe bloody dysentery. There had recently been some pain through the region of the liver. *Endamæba histolytica* was identified in the stool. Treatment consisted of a total of 10 grains of emetin, hydrochloric acid, and coal-oil enemas. He was dismissed from observation, but neglected to finish the emetin course, 4 grains still remaining. Three weeks after the course of emetin was terminated severe pain developed in the right lower thoracic region. His physician opened a large abscess which drained for three months. Defecation has occurred only once daily. From the draining abscess smears were made and *Endamæba histolytica* was identified in numbers by Magath. Better drainage was provided and treatment with emetin again instituted. The abscess cavity was irrigated with

quinin hydrochlorid. After a fairly uneventful postoperative course the wound healed. A series of stool examinations was negative for the endameba. The patient was examined again one year later because of severe dysentery of three weeks' duration and pains throughout the abdomen. The ameba was again found and the proctoscopic examination revealed characteristic amebic proctitis. Following another course of emetin he was sent home to take bismuth for a month. Two months later the stool still contained the ameba and a course of salol and ipecac was begun. At the conclusion of this treatment a series of six stools was negative. He was seen again six weeks later and reported no further trouble.

Amebic abscess of the liver is a rare complication in the North Temperate Zone. The source of the infection in this case is not known, but the symptoms had been evident for only four months, although the patient had been in Montana for several years. Many authorities have observed that abscess develops rarely in treated cases; it is in those of long standing with little or no treatment that this complication is more likely to occur. The patient had neglected to complete an adequate course of treatment, with the result that the liver was invaded. He eventually made a good recovery and seemed to be free of the parasite.

During the last seven years there have been very few proved cases of amebic abscess of the liver at the Mayo Clinic. There have been four cases in which the ameba was found in the pus from the liver. In three other cases in which abscess was drained amebæ were not found in the smears from the abscess, although they were identified in the stool. Drainage and anti-amebic treatment brought about recovery in all. In another case abscesses had been drained on three occasions and the patient feared the development of a fourth abscess. The ameba was identified in the stool and suitable treatment relieved all symptoms. These eight cases are the only proved or partly proved cases of amebic abscess of the liver in the Mayo Clinic in seven years. The actual percentage cannot be ascertained, but certainly it is only a fraction of 1 per cent of all cases of infection by *Endamæba histolytica*.

In the last four years operation has been performed in nine cases of hepatic abscess. In these cases the ameba was not

held to be the etiologic factor. It would seem that some infection other than the parasite is the more common cause of hepatic abscess in the North Temperate Zone.

Case 3.—The patient, a man aged thirty-five, came from British Columbia. One year previously he had had an attack of fever and chills, followed in two days by abdominal pains and diarrhea. The illness persisted for two weeks. Since then this trouble had recurred at intervals of from seven to ten days. Treatment along nonspecific lines had been unavailing. He had lost 30 pounds. Pus, blood cells, and *Endamæba histolytica* were found in the stool. Proctoscopic examination showed that the mucosa bled with slight trauma. So far as could be seen the mucosa was studded with umbilicated, punched-out ulcers. A roentgenogram of the colon after a barium filling enema was negative. In the course of two weeks 10 grains of emetin hydrochlorid was given hypodermically and twenty-four treparsol tablets. There was definite improvement. At the conclusion of this regimen examination of the stool on three successive days did not disclose ameba. On proctoscopic examination it was found that the ulcers had entirely disappeared, but the mucosa was reddened, thickened, granular, bled on slight trauma, and was diffusely involved. Cultures were obtained from the rectal mucosa and a rich growth of the Bagen diplococcus was obtained. Vaccine treatment was then instituted.

This case is an excellent example of the coincidence of two diseases. The endameba was found to occur in 10 per cent of cases of chronic ulcerative colitis, as determined by Bagen of the Mayo Clinic. It is a coincident infection and not the cause of chronic ulcerative colitis. Unless this fact is recognized a favorable result cannot be obtained in the treatment of such cases. If the patient will tolerate treparsol it is usually combined with emetin. There is usually some definite benefit from this treatment, particularly if the rectal mucosa shows the umbilicated, punched-out lesions so characteristic of amebic activity. An autogenous vaccine is administered at the same time. It has been a fairly frequent observation that ulcerative colitis may be made worse by the administration of any organic arsenical compound, and this fact may serve to indicate the association of ulcerative colitis in a case of amebic colitis or that there has been an error in the diagnosis.

Case 4.—The patient was a woman aged thirty-seven, from Iowa. Diarrhea had persisted steadily for one year. The stools varied from four to

five daily and occurred chiefly between 5.00 and 7.00 a.m. They were watery, light in color, tended to float, had a foul odor, and did not contain blood. There was but little abdominal pain, although much flatulence. Urgency was marked. At times glossitis and stomatitis were present. The patient was 15 pounds below her normal weight. The blood count was normal. The total gastric acidity was 42, and the free hydrochloric acid 20. *Endamæba histolytica* was found on two examinations of the stool. Roentgenograms of the stomach and colon were negative. The sigmoidoscopic examination was negative. Because of the presence of the ameba a course of stovarsol was given. There was moderate improvement. A series of examinations of the stool was now negative. Following this the symptoms recurred and arsenicals and emetin were of no help. Following a period at home the patient returned to the Clinic and reexamination of the stool was negative on three successive days. Calcium lactate and parathyroid tablets were then given. The diet was chiefly high-protein and high-vitamin in character. At the end of six months the patient had regained her normal weight and her general health was much improved. An occasional spell of diarrhea and stomatitis still occurred, but it did not interfere with her ability to work.

Two definite points may be emphasized in this case. The more important one is that the endameba may be present and yet bear little or no relation to the cause of the dysentery. The proctoscopic examination and the roentgenogram of the colon eliminated ulcerative colitis. There was no achlorhydria to explain the symptoms. At the first examination the presence of the ameba was overemphasized, while the significant points were all but disregarded, namely, the character of the diarrhea, the condition of the mouth, and the inconclusive response to specific treatment. It is most unusual to find a case of endamebiasis that does not manifest marked, even though transitory, response to proper treatment. There is no question that antiamebic treatment should be administered as in this case, in which it has seemed to be successful in eradicating the parasite.

At the patient's second visit, several months later, the salient features of the problem were properly evaluated. This was not a "nervous diarrhea," nor did it conform to any ordinary disease entity. There were certain features that suggested a deficiency disease. There were not enough data to warrant a diagnosis of sprue or pellagra, but there was enough vague similarity to justify treatment suitable for deficiency of this general nature. The patient was instructed along such lines as would insure a

high vitamin content in the diet. The rôle of calcium and parathyroid is on an empiric basis and their value in the case is uncertain. After six months of this regimen a favorable clinical result had been obtained. The condition is not cured, but the patient is so markedly improved that she considers herself entirely adequate to carry on efficiently.

I am not prepared to make a positive diagnosis, but suggest that this is a type of indeterminate diarrhea further observation of which may justify its classification under the heading of "deficiency diarrhea."

SUMMARY

There is yet no infallible therapeutic measure in the treatment of endamebiasis. At the present time treparsol, stovarsol, yatren, and emetin seem to be the most effective remedies.

Emetin is most effective in controlling the acute stages, but should be accompanied or followed by one or more of the other drugs. Persistence in treatment and repeated examinations are essential to cure.

Amebic abscess of the liver is a rare complication in the North Temperate Zone. This parallels the frequent observation that severe types of amebic colitis are less common in the north.

Amebic colitis and chronic ulcerative colitis may occur in the same case. Each disease must be recognized before cure can be effected, as there is no etiologic connection between the two diseases.

Coincident amebic infection during an attack of "indeterminate" diarrhea may cause temporary uncertainty as to the diagnosis. Anti-amebic treatment is always indicated, but usually has very little effect on the symptoms.

CASES FROM THE SECTION OF LEDA J. STACY

PRECOCIOUS PUBERTY.....	LEDA J. STACY
ANOMALIES OF THE FEMALE GENERATIVE TRACT (FOUR CASES).....	L. MARY MOENCH
HYPERTROPHY OF THE BREASTS.....	SUSAN R. OFFUTT
ADENOMYOMA OF THE UTERUS IN YOUNG WOMEN (TWO CASES).....	DELLA G. DRIPS
PROLAPSE OF UTERUS IN A YOUNG WOMAN.....	DELLA G. DRIPS

PRECOCIOUS PUBERTY

Case 1.—A girl eleven years of age was brought to the Clinic because of abnormal physical development and recent slight changes in personality. The child developed normally, walking and talking at the usual age and the teeth erupting at the usual time. During the second year a permanent squint developed which was corrected by glasses, and the strabismus has not changed since, although glasses were changed frequently until three years ago; they have not been changed in the last three years. When the child was about two years old the mother noticed an occasional bloody discharge from the vagina, and at the fifth year regular menstrual periods were established and have remained regular, lasting four or five days and accompanied by slight dysmenorrhea. The child developed rapidly until the age of six or seven years, when she wore clothing of a size for a twelve year old; she then ceased growing and still wears the same size clothing as at seven years of age, although she has gained in weight. She started school at five and has been studious and bright. She has always been at the head of her class and is now in the seventh grade. Her father believes she has shown some evidence of deterioration during the last six months, as she has become more sensitive, more easily disturbed emotionally, and does not play with her classmates as formerly. During the last two months the child has had daily frontal headaches, occurring at about 3.00 p.m. and lasting for three hours. During the last two years she has experienced slight momentary dizziness. At the age of one and a half years she fainted on two occasions. The child now occasionally becomes pale for from three to five minutes, but there never have been convulsions.

The child was active, alert, smiling, and coöperated in all examinations. The fingers were short and tapering. Systolic blood pressure was 103 and diastolic 70. The teeth were irregular. The breasts were developed and axillary and pubic hair present as in an adolescent girl. The hips were broad and buttocks prominent as in an adult of forty years and a fine lanugo was present over the trunk, buttocks, and extremities. The hymen admitted one finger, the cervix and uterus were of adult size, and the ovaries were appa-

rently of normal size; tumors were not palpable. The general examination was otherwise negative. Urinalysis and examination of the blood, including a blood Wassermann test, were negative. Neurologic examination was also negative. The basal metabolic rate was -17 . Roentgenograms of the chest, head, hands, sella, kidneys, ureters, and bladder were negative.

A diagnosis of *pubertas præcox* was made. Because of the low basal metabolic rate the patient was given desiccated thyroid. There is no family history of maldevelopment. The general contour of the patient's body suggested pituitary dyscrasia.

In 1922 Reuben reviewed from the literature 398 cases of precocious puberty and added eight of his own. One hundred eighty-eight of the 398 were females. Sixty-four came to operation or necropsy. He calls attention to the distinction between precocious menstruation and precocious puberty, noting in the latter precocity involving the entire body, characterized by rapid development of the body in height, weight, and volume, the premature appearance of regular ovulation and premature development of external genital organs, whereas in precocious menstruation, menstruation may occur between the first and seventh year, then may cease and return at the usual time of puberty coincident with normal development of the body.

In the 188 cases of precocious puberty in females malignant tumors of the ovary are known to have been present in twenty-three. In seventeen, tumors of the suprarenals were found; the internal genitalia were enlarged in only one of these cases. Twenty cases of tumor of the pineal gland in children coming to necropsy have been reported in the literature. Precocious puberty occurred in only seven and in every case the patient was a male.

Reuben believes that the only glands which primarily induce permanent sexual precocity are the suprarenal, the pineal gland, and the gonad, and that such precocity is largely a polyglandular syndrome. Goetsch, Smith, and others, however, believe that hyperactivity of the hypophysis stimulates the development of the sexual glands.

The etiology of precocious puberty will be in question until more is known of the interrelationship of the endocrine glands.

ANOMALIES OF THE FEMALE GENERATIVE TRACT

Case 2.—A woman aged thirty-three registered at the Clinic July, 1927. The complaint was right inguinal hernia which had been present since her earliest recollection. There had been no history of strangulation and there were no subjective symptoms relative to the hernia. She complained of never having menstruated; she had been married seven years and was desirous of children. She had been told that there was an abnormality in the development of the internal generative organs, and she stated that she had two aunts whose condition was similar, who had never menstruated and who also had inguinal hernias.

The patient appeared to be a fairly well-developed young woman. The breasts were normal. There was a masculine type of distribution of hair and of adipose tissue. Examination of the pelvis revealed a normal vagina, but the cervix was absent and the fundus uteri could not be found. There was, however, a small firm mass just beyond the apex of the vagina which was somewhat of the consistence of bowel. The ovaries could not be palpated. In view of the congenital abnormality it was thought that the hernia might contain a sex gland, although this could not be determined by palpation. Her habitus had been considered that of a female and she regarded her sex reactions as normal.

At operation the hernia was opened and was found to contain a sex gland, which on investigation proved to be a testicle, and was removed. According to the definition of the term, this case would be classified as pseudo-hermaphroditism.

Case 3.—The sister of the patient in Case 2, a married woman aged twenty-two, came to the Clinic August 30, 1927. She had never menstruated; she had been married two years and desired children. At the age of seventeen she had been greatly troubled by hot flashes which had in time disappeared. She had never had any sense of pelvic congestion or any indication of menstrual activity. She stated that her marital relations had been normal in all respects. She complained also of nervous irritability and said that she was easily nauseated and had frequent transient headaches. Her weight during the adolescent years had been excessive, the average being 150 pounds. During the last few years this weight had gradually readjusted itself and was now constant at 136 pounds. She was 64.5 inches in height. General examination was essentially negative except for the pelvic organs. The external genitalia were normal. The vagina was very short, measuring 5 cm. No cervix or fundus could be made out; the ovaries were not palpable.

The appearance of the hot flashes and the vasomotor instability of the adolescent years suggest premature menopause. It is possible that ovaries may have begun to develop independently, but owing to failure of reciprocal action with the uterus had undergone spontaneous atrophy. The habitus of this patient was that of a female in all respects, and the condition might readily be interpreted as failure of the development or atresia of the müllerian ducts. It is difficult to explain the presence of the vagina on the basis of this theory.

Case 4.—A woman aged twenty-one registered at the Clinic August 30, 1927, complaining of fatigue and generalized muscular aching. She had never menstruated and she had been married for two years and had not become pregnant. She stated that she had four sisters, two of whom menstruated normally at the usual time and the remaining two were still in the preadolescent years. She had been told that a great aunt had not menstruated, but was not certain as regards this. She stated that her sexual reactions were normal, although there was some dyspareunia. She complained a great deal of nervousness and stated that she was emotionally unstable at times. This patient was 64 inches tall and weighed 160 pounds, was well developed, and her habitus was that of a female. Pelvic examination revealed a vagina small in all diameters. There was no evidence on bimanual examination of either a cervix or fundus and the ovaries could not be felt.

Case 5.—A woman aged nineteen registered at the Clinic July 18, 1927, complaining of failure to menstruate and of moliminal symptoms consisting of a sense of congestion throughout the pelvis lasting about three days each month since the twelfth year. A year previously examination elsewhere

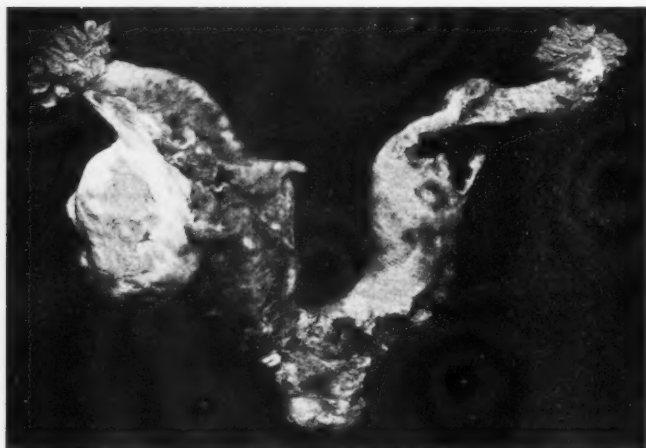


Fig. 238.—Ribbon uterus.

had revealed atresia of the vagina. Following this a plastic operation on the vagina was attempted. After operation there was bleeding for ten days, but the periodic pelvic symptoms were not altered.

The patient was somewhat overweight. General examination was negative in all respects except for the pelvis. The external genitalia were normal. The vagina admitted two fingers for about 4 cm. and by rectum a small conical ridge was felt, probably a small cervix, but the fundus could not be

outlined. There was a definite history of chronic appendicitis, and in view of this and the pelvic complaint exploration was advised. At operation a congenital anomaly of the internal genital organs was demonstrated. There was a bilateral ribbon uterus joined at the cervix (Fig. 238). Each half of the uterus was dilated with blood (hematometra). The tubes were apparently normal. The right ovary was about three times normal size as result of multiple cysts. On this account the right ovary as well as the appendix was removed, and total abdominal hysterectomy was performed. Figure 238 shows the anomalous condition of the internal generative organs. The condition in this case is due to failure of fusion of the müllerian ducts beyond the cervical canal resulting in true uterus didelphys of the ribbon type.

HYPERTROPHY OF THE BREASTS

Case 6.—An unmarried woman aged nineteen came to the Clinic July 1, 1926, complaining of enlarged breasts and obesity. She had weighed 175 pounds at the age of twelve, and a year previously had weighed 214, but had reduced to 191. Menstruation began at eleven and periods were regular and normal since the onset. The mother stated that the daughter had had large breasts since puberty. Her general health was good. She was active, but felt the inconvenience of the breasts and obesity in athletics and was sensitive regarding her appearance.

On examination the skin was moist and warm. There was moderate hypertrichosis of the face; except for the breasts the general examination was negative. The right breast was larger than the left. In the standing position the lower margin of the right breast was 1 cm. above the level of the middle of the umbilicus and the lower margin of the left breast was 5 cm. above the umbilicus. There was no mastitis. July 13 and 14, August 31, September 1, and November 6, 1926 the patient was given roentgen-ray treatment (voltage, 135; distance, 16 inches; filtration, 4 mm. aluminum; milliamperes 5, and time, twenty minutes). The patient meanwhile reduced her weight to 176.5 pounds, but there was no appreciable reduction in the size of the breasts. Moist compresses of saturated solution of magnesium sulphate over the breasts at frequent intervals and the use of a brassiere were employed during the year of observation without effecting a reduction in size of the breasts.

July, 1927 the patient returned and desired amputation of the breasts, stating she was greatly inconvenienced by them. The examination was essentially the same as on previous visits.

Bilateral simple amputation through transverse incisions was performed. The weight of the breasts was 1,587 gm. and 1,700 gm. and the hypertrophy was due to fatty tissue (lipomatosis). Convalescence was normal and the wounds were practically healed in three weeks.

This is a case of noninflammatory and nonneoplastic hypertrophy of both breasts. The hypertrophy is largely the result of an increase in the fatty tissue with slight hypertrophy of the

mammary gland, and may be termed lipomatosis or adiposity of the breasts. The cause is unknown, but dysfunction of the endocrine system is believed to be associated with it. Conservative measures are usually ineffectual, particularly in extreme cases, and in most cases amputation is warranted.²

ADENOMYOMA OF THE UTERUS IN YOUNG WOMEN

Case 7.—An unmarried woman, aged thirty, teacher by occupation, registered at the Clinic July 19, 1927. She complained of vaginal bleeding which had been almost continuous for seventeen years. When the patient was twelve years of age menstrual flow began to appear at irregular intervals. There was never a definitely established menstrual cycle. After the first year the vaginal bleeding occurred daily, varying from a few drops to profuse hemorrhage. This did not cause great weakness or pallor, but occasionally the patient was dizzy and had to spend a day or so in bed. Once, in 1916, the "hemorrhages" became so profuse that she had to give up teaching. In 1919 curettage stopped the flowing for two years; however, it gradually became almost constant again as it was when she came to the Clinic. She was leading an active out-of-door life and none of her activities seemed to influence in any way the amount of bleeding. There was no pain. There was no personal or family history of bleeding other than this.

The general examination was essentially negative except for the pelvic condition. Pallor of the mucous membranes was not observed. The uterus was twice the normal size with distinctly rounded contour anteriorly, giving the impression of a fibromyoma. The hemoglobin was 70 per cent; the blood Wassermann test was negative, the coagulation and the bleeding times were normal, and the platelet count averaged 112,000. Uterine fibromyoma was diagnosed, but it was noticed at the time that the history was atypical for fibromyoma. Curettage with abdominal exploration to follow was advised. Before operation insufflation of the tubes and injection of 40 per cent iodized oil showed both tubes to be obstructed. No history of pelvic infection was obtainable.

Curettage revealed nothing of consequence within the uterine cavity and the abdomen was opened. The uterus was about twice normal size. There was an adenomyoma in the fundus of the uterus involving both tubes. The fundus of the uterus was excised with a small part of each tube; the distal part of the tube was transplanted into the endometrial cavity, and the uterus was closed. Nothing unusual was noted about the ovaries. The pathologist reported fairly diffuse adenomyoma and polypoid endometrium.

Case 8.—An unmarried woman aged twenty-three registered at the Clinic on August 1, 1927, complaining of profuse and painful menstruation. The menstrual periods had always lasted a week and bleeding had been profuse. The menstrual cycle was established at thirteen years, was regular, and there had never been any intermenstrual bleeding. The patient had always suf-

ferred from cramps during the first two days of the period, usually necessitating remaining in bed for the first day. In February, 1927 she noticed that she passed clots for three or four days. Gradually bleeding had become more profuse at each period, so that the patient could not be on her feet for the whole week. She felt that she was growing weaker after each period. The menstrual cramping had increased in severity with the increased flow. She had no other complaint.

General examination was essentially negative except for some pallor of the mucous membranes. The uterus was retroverted, of normal contour, about normal in size and quite movable; the adnexal regions seemed normal. The hemoglobin was 55 per cent, erythrocytes numbered 3,910,000. The coagulation and bleeding times were normal, and the platelet count was 164,000. The blood Wassermann test was negative.

Submucous fibromyoma was diagnosed, and curettage and examination under anesthesia advised. On examination, under anesthesia, the uterus seemed twice as large as normal. Very little material could be obtained with the curet, and it was thought advisable to open the abdomen. There was an adenomyoma in the fundus of the uterus and when the uterine cavity was opened polypoid endometritis, graded 3, was found. Practically no polypoid tissue had been obtained by curetting from below. The adenomyoma was removed and internal shortening of the round ligaments was performed. The pathologic report was chronic hypertrophic endometritis and adenomyoma.

In both of these cases there is a cause of uterine bleeding in younger women which is not usually considered. Uterine adenomyomas, according to reports in the literature most commonly produce symptoms in the fifth decade. The average age at which they occur is given as forty-one years. Metrorrhagia or irregular bleeding such as the first patient complained of is also uncommon with adenomyoma of the uterus. Usually menorrhagia only is present and the hemorrhages, which are quite characteristic, occur with the periods. Pain during the periods is usual; in the first case the patient did not complain of pain. Adenomyoma of the tubes must also be thought of in cases of tubal obstruction in young women, especially when there is profuse bleeding and pain during the periods or some irregularity of menstruation. Adenomyomas of the uterus are often more difficult to detect on physical examination than fibromyomas because the normal contour of the uterus is usually retained.

PROLAPSE OF THE UTERUS IN A YOUNG WOMAN

An unmarried woman aged forty-one, a Russian Jewess, and a tailoress by trade, registered at the Clinic August 3, 1927. She complained of displacement of the womb. She said that at the first menstruation at the age of fifteen "something came down outside" of the vulva which she thought was hard and red and the size of a fist. It disappeared within the vagina until the next period, then it reappeared larger than before. At this time she was working in a bakery in Russia where she had to squat on the floor and lift large pans of bread from low ovens. After the third month an operation was performed but was not successful, and a second operation was necessary before the patient left the hospital. After she had been back at work again for about a month "it came out again" and has been out ever since. She changed her occupation and became a tailoress. Two years ago, twenty-three years after the first operation, "some stitches broke" and "something came out the size of a finger" and has remained out continuously unless manually replaced. The menses have always been regular and normal, but for the last two and a half years the patient has noticed some intermenstrual spotting. She has had very little leukorrhea and no abdominal pain.

The patient was very self-conscious and apparently her trouble had influenced her life greatly. She said she had never told even her mother or sisters of it, and had never married on account of it.

The general examination was essentially negative except for dental caries and many crowned teeth. On inspection of the vulva, a red finger-like polypoid mass was seen protruding from the introitus. With straining the cervix came outside the introitus about 4 cm. and the protruding mass was recognized as an ordinary cervical polyp. It was about 5 cm. long and bled on the slightest manipulation. Bimanual examination showed the uterus to be about normal size and in median position. The cervix was slightly elongated but there was definite prolapse of the fundus. The surgeon advised removal of the polyp and uterine suspension. The patient wished only the removal of the polyp, which is not strange, as the former operations had failed. She was quite satisfied after the operation, so evidently it was the polyp that had troubled her and resulted in her visit to the Clinic. She had become accustomed to the prolapse and could get along with it because her occupation allowed her to sit much of the time. The early appearance of prolapse and its influence on the patient's life are features of universal interest.

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PREËCLAMPTIC TOXEMIA

ROBERT D. MUSSEY

A WOMAN aged twenty-three, pregnant for the third time, was referred to the Clinic by her physician November 4, 1927. She had two children four and two years of age. Both pregnancies had been uneventful. There was no history of toxemia, edema, or albuminuria. The first delivery was instrumental and the second spontaneous and of short duration. She had nursed the last baby for about fourteen months and had not menstruated since the baby was born; she thought pregnancy was nearly at full term. She had had no prenatal care and had consulted her home physician that day for the first time on account of a severe headache which had been present for a week. He found marked albuminuria and high blood pressure (systolic about 180), warned her of the impending danger of eclampsia, and advised her to go to a hospital.

The patient was pale. Slight edema was present. She weighed 138 pounds, having gained 25 pounds during pregnancy. The systolic blood pressure was 154 and the diastolic 98. A dose of Epsom salts had been taken that morning, resulting in free catharsis which probably caused the lowering of the blood pressure. There had also been abdominal cramps, but she was not sure that these were associated with uterine contraction. The uterine fundus was about 33 cm. above the pubes and the fetal head was in the pelvic inlet. Fetal heart tones were heard in the left lower abdominal quadrant. The cervix was practically effaced and admitted the tip of one finger. The blood urea was 33 mg. and the blood chlorids were 62 mg. for each 100 c.c. The carbon dioxid combining power was 48 per cent.

As the blood pressure did not seem alarmingly high, the patient was given $\frac{1}{4}$ grain of morphin as a sedative and for relief of the severe headache. By noon of the following day the blood pressure had risen to 198 systolic and 110 diastolic, and the intense headache had recurred. As these symptoms indicated impending eclamptic convulsions, it was thought advisable to induce labor. At 5.30 p.m., a No. 5 Vorhees' bag was inserted into the lower uterine segment, and the patient was given $\frac{1}{4}$ grain of morphin in 2 c.c. of 25 per cent chemically pure magnesium sulphate intramuscularly. The labor pains which were initiated came with increasing frequency, the bag was expelled three hours later, and a living baby, weighing 5 pounds, 10 ounces, was delivered spontaneously at 9.30 p.m. Convalescence was uneventful. One day postpartum the blood pressure had dropped to 170 systolic and 95 diastolic, and nine days later it was 112 systolic and 70 diastolic.

The patient's diet of 1,500 calories with 50 gm. of protein and low in

salt was adequate to allow her to nurse the baby. As there was little edema, she was given at least 1,500 c.c. of water daily. She was kept in bed until the blood pressure approached normal and the albuminuria was greatly lessened. She was urged to continue a somewhat similar diet for several months until general condition, blood pressure and urine were normal.

This case illustrates the importance of prenatal examinations, and the significance of the signs of the onset of toxemia of the later months of pregnancy, and the conduct of cases of pre-eclamptic toxemia.*

It may seem superfluous to reiterate the necessity for routine examinations during pregnancy. There has been a definite decrease in morbidity and mortality in all groups in which prenatal examinations and care have been carried out as a routine. However, 25 per cent of the deaths during pregnancy and confinement are still due to the toxemia of the eclamptic type, and it is evident that the laity and, to some extent, the medical profession have not been convinced completely of the value of this care.

Each patient should be examined early in pregnancy and should be advised in regard to diet and general hygiene, including elimination and exercise. It has long been thought that a diet high in protein is likely to cause a disturbance of the kidneys during pregnancy, even the development of pre-eclamptic toxemia. More recently, clinical investigation has shown that abnormal gain in weight due to the ingestion of too much food, and an increased intake of sodium chlorid may have as much, if not more, to do with the development of pre-eclamptic toxemia than a diet high in protein. However, the protein intake should be watched, and decreased if albumin is found in the urine.

Aside from the opportunity for giving advice to the patient, the chief occasion for prenatal examination as a routine is for the early detection of the signs of toxemia. If this patient had consulted her physician sooner, he might have found evidence of toxemia and have been able to avert it. Three symptoms indicate the approach of toxemia: (1) albuminuria, (2) rising blood pressure, and (3) unusually rapid gain in weight, with or without

* The term "pre-eclamptic toxemia" is used to cover so-called true eclampsia as well as nephrosis or nephritis of pregnancy.

edema. It is true that small amounts of albumin in the urine of pregnant women may be of no consequence, and that albumin may be evidence of an inflammatory condition in the kidneys or bladder rather than of preëclamptic toxemia. However, definite albuminuria with gradually rising blood pressure and edema or undue gain in weight are evidence of toxemia. When headaches, visual disturbance, dizziness, and epigastric pain are also present, grave preëclamptic toxemia has developed.

If patients gain too much weight during pregnancy, symptoms of toxemia may develop. Randall showed a definite rapid rise in the plotted curve of gain in weight in cases in which toxemia developed, in comparison with the more gradual rise in the curve of gain in weight in the normal cases. The diet should be regulated so as to limit the gain in weight to not more than 20 to 25 pounds during pregnancy.

With the appearance of any of the signs of developing toxemia, the patient should be advised to follow strict dietary rules. Protein in the diet is limited to not more than 50 gm. daily, and the total intake of food is reduced sufficiently to stop gain in weight or to reduce the weight until the condition improves. The intake of salt is reduced to a minimum; the patient is urged to take saline laxatives if necessary in order to have free daily catharsis. The patient should be impressed with the fact that activity tends to increase the albumin in the urine and to raise the blood pressure.

If in spite of care the patient grows worse she should be put to bed, preferably in a hospital. The carbon dioxid combining power should be determined to indicate the presence or absence of acidosis; blood chlorids should be estimated if the patient is edematous, and the nonprotein nitrogen partition should be investigated to determine whether or not there is retention of urea. Examination of the ocular fundi is of value, particularly in revealing evidence of previous nephritis. Treatment depends on the character and severity of the symptoms and the rapidity with which they progress. The patient should be kept in bed on a diet, containing approximately 1,500 calories with a low protein content (about 50 gm.), and a minimum of

salt. If edema has developed, the daily fluid intake should be limited to from 800 to 1,000 c.c. until the edema has decreased or has disappeared.

The disappearance of edema may be accelerated by the use of diuretics. Ammonium chlorid (as much as 10 gm. daily), in divided doses in gelatin capsules containing 1.5 gm. each, causes marked diuresis. Ammonium nitrate in 0.5 enteric-covered pills has more recently been used to effect the same result. Lazard and others have obtained a similar result with 10 c.c. of a 20 per cent magnesium sulphate solution intravenously or intramuscularly. These diuretics are of distinct value, and in a group of cases under my care the use of ammonium chlorid was followed by prompt diuresis, disappearance of edema, marked loss of weight, lowered blood pressure, and general improvement. In many cases the improvement thus produced made it possible for pregnancy to be continued until a living child could be delivered. These drugs should be used with caution when there is urea retention or when the carbon dioxide combining power of the blood is reduced.

The patient came to the clinic with eclamptic convulsions impending. The high blood pressure and marked albuminuria were evidence of advanced toxemia. She also had severe and persistent headache which, under similar conditions, is frequently the premonitory symptom of eclamptic convulsion. The edema was slight. It has been a clinical observation that eclamptic convulsions may be more severe and harder to control in a patient with little or no evident edema. The blood pressure of this patient was only moderately high on admission but rose to 198 systolic and 110 diastolic in the next eighteen hours. The height and size of the uterus indicated that the patient was in the last month of gestation.

Two courses of management may be considered: (1) expectant treatment, including sedatives, diet, and the production of proper elimination, and (2) measures to terminate the pregnancy by induction of labor or rapid emptying of the uterus. If this patient had not had the severe headache, I probably would have given her a large dose of castor oil both for its cathartic

action and for the chance that it might induce labor pains. Had this improved her condition without induction of labor, expectant measures would probably have been instituted. If she had reached the convulsive stage of toxemia and had not been in labor, measures would have been instituted for the control of the convulsions before the pregnancy was terminated.

If termination of pregnancy is necessary, one of several procedures may be chosen. The improvement in surgical technic in recent years has broadened the field for cesarean section; many obstetricians believe that the field has become too broad. Abdominal cesarean section may be performed in order to terminate pregnancy in cases of severe preëclamptic toxemia or eclamptic convulsions. Certain statistics show that the margin of safety for the patient is increased if the toxemia is controlled before the patient is subjected to the shock of major surgical procedures which put an increased load on kidneys already overtaxed. The toxemic symptoms in this case had not gone beyond the limits of control. Labor in the patient's last pregnancy had been spontaneous and rather rapid. If she had been pregnant for the first time under the same conditions, abdominal cesarean section might have been advisable, but as she was a multipara it was thought that labor would be relatively rapid after it had begun. The insertion of the Vorhees' bag to induce labor was chosen rather than podalic version because manual dilatation of the cervix followed by version (*accouchement forcé*) offered greater chance of harm to this patient both by injury to the tissues and by shock.

When the patient was dismissed from the hospital she was advised to be examined after a year to determine if the renal function has returned to normal. If at that time there is evidence of edema or hypertension and if albumin is present in the urine, further tests are advisable. Increase of urea or the nonprotein nitrogen partition in the blood or the prolonged retention of the phenolsulphonephthalein is evidence of lowered renal function. When renal function is seriously impaired, the specific gravity of the urine is relatively fixed. With a dry diet the urine of a normal person will be concentrated and the specific

gravity should rise to 1.025 or more; conversely, following the drinking of a quantity of water in a short time, the specific gravity of the urine should be distinctly lowered.

The doubtful case should be studied in the hospital. The patient should be kept in bed on a prescribed diet and fluid intake for several days. The blood pressure should be recorded, the ocular fundi examined, the output of urine measured, the phenolsulphonephthalein test of renal function made, and the nonprotein nitrogen partition in the blood determined. The upper and lower limits of the specific gravity of the urine should be determined. For the concentration test, the patient is given a diet for a day consisting of 20 per cent solid food only; no fluids are given. The urine is collected at three-hour intervals. The specific gravity should reach 1.025. For the water test, 1,500 c.c. (seven and a half glasses) of water is given on an empty stomach between 8.00 and 8.30 a.m. The urine is collected at half-hour intervals for four hours. The normal output varies between 1,200 and 1,800 c.c. and the specific gravity should be at least as low as 1.003.

The results of these examinations will show either that the patient has completely recovered or that there is more or less impairment of renal function as a result of chronic nephritis. With this evidence at hand it is possible to give the patient better advice about treatment and care in subsequent pregnancies.

OCCIPUT-POSTERIOR PRESENTATION

LAWRENCE M. RANDALL

THE case presented here, that of a primipara in the second stage of labor, illustrates a common obstetric complication: premature rupture of the membranes with engagement of the occiput in the posterior half of the pelvis and failure of rotation to the anterior. The patient, aged thirty-two, registered for prenatal care in the fourth month of gestation. Her height was 5 feet, 4 inches, and she weighed 124 pounds. General examination revealed dental caries and one tooth showed considerable periapical infection. The tonsils had been cleanly removed. The breasts were pendulous with poorly developed nipples. The fundus uteri was palpable above the pubis. The laboratory examinations including the Wassermann test on the blood were negative. The pelvic measurements were: interspinal, 23 cm.; intercrystal, 28 cm.; bitrochanteric, 31 cm.; Baudelocque, 20 cm.; pubococcygeal, 8.5 cm.; and the distance between the ischial tuberosities, 9 cm. There was a good arch at the outlet. The coccyx was less mobile than usual. The spines of the ischium were rather prominent. There was a normal sacral curve and the promontory could not be reached.

The routine antenatal instruction was given the patient, and she was advised to consult a dentist. Two weeks prior to the expected date of confinement the abdomen and pelvis were examined. At this time the fetus was presenting by vertex, back to the right, with the head engaging in the transverse diameter of the pelvis. The cervix was fairly well effaced and closed.

Four days before the provisional date of labor, the membranes ruptured with the onset of pains and the patient entered the hospital. The systolic blood pressure was 138 and the diastolic

80. The weight was 150 pounds. There were uterine contractions every eight minutes, lasting for thirty seconds. There was no bloody show but considerable liquor amnii was escaping. Abdominal palpation revealed the back to the right flank and small parts easily palpable to the left of the median line. The anterior shoulder was felt just to the right of the median line, 6 cm. above the pubis. The vertex was firmly engaged, probably in the right posterior quadrant. The fetal heart tones, 144 to the minute, could be heard best in the right flank. Rectal examination showed complete effacement of the cervix with 1 cm. dilatation, and the external os posterior and to the right.

The usual preparation, including a cleansing enema, was given and the patient was instructed to lie on the left side to favor rotation as labor progressed. The pains gained in severity and nine hours after the onset were from forty-five to fifty seconds in duration with intervals of three minutes. There was dilatation of 3 cm. The patient complained considerably of the pains, particularly in the lower part of the back. At this time, $\frac{1}{6}$ grain of morphin in 2 c.c. of sterile magnesium sulphate (25 per cent) was given intramuscularly. The administration was succeeded by three hours of comparative comfort; the contractions occurred every five or six minutes and were vigorous but less painful, and in the interval the marked backache was less. At the end of three hours she was again complaining bitterly of the pain and backache. Uterine contractions occurred every two and a half or three minutes and lasted for fifty seconds. Rectal examination showed dilatation of 5 cm., vertex in midpelvis and the sagittal suture palpable in the right oblique. As twelve hours had elapsed since the administration of the cleansing enema, another was given and preparations made for oil-ether-colonic analgesia.

The instillation in this case was completed thirteen hours after the onset of labor. Fifteen minutes later the patient was oblivious to her surroundings, stirring and moaning slightly with the uterine contractions. Satisfactory results from the oil-ether-colonic instillation continued for four hours, at the end of which time there was complete dilatation of the cervix; the vertex

had descended to the level of the ischial spines with the sagittal suture still in the right oblique diameter of the pelvis. Palpation, however, revealed considerable molding of the cranial bones. Inasmuch as the patient was in the second stage of labor, the colonic analgesia was not repeated, but nitrous oxid and oxygen was administered by inhalation and the patient instructed in bearing down. She coöperated well and definitely increased the molding, although the occiput still remained behind the transverse diameter. After eighty minutes had elapsed without progress in rotation or descent, interference was decided on. A careful vaginal examination showed that the perineum was rather snug. There was considerable overlapping of the cranial bones; the sagittal suture was in the right oblique, the small fontanel posterior on the right and the large fontanel anterior on the left; the cervix was completely dilated and effaced. Pushing up the head, I located the posterior ear and verified the previous observations and diagnosis. The cord was discovered once around the neck. The capacity of the pelvis was normal save for slight contraction of the outlet. Mother and babe were in good condition.

The bladder was emptied with a catheter and the external genitalia were liberally douched with lysol solution. The hand whose palm encountered the occiput was introduced (in this case, the left) into the vagina. The fingers were carried back of the babe's right mastoid process, and in conjunction with a uterine contraction and the coöperation of the patient attempt was made to rotate the occiput anteriorly. This manipulation was repeated with several pains, but to no purpose. The anesthesia was deepened; I pushed the vertex up until my hand slipped by and encountered the posterior shoulder to the left of the sacral promontory. Still further disengaging the head, aided by manipulation with the other hand, I carried the shoulder to the right of the promontory, so that the back was anterior. The head was led back into the pelvis with the occiput in the left anterior quadrant. It was important to carry the occiput to the left occiput-anterior position instead of the right occiput-anterior position. The pelvic soft parts had been

accommodated to the long diameter of the head in the right oblique where it still remained when converted from the right occiput-posterior position to the left occiput-anterior position. Conversion to right occiput-anterior position often leads to return to the right occiput-posterior position.

At this point anesthesia might be reduced to allow the patient to complete the labor by bearing-down effort, or a low-forceps operation and episiotomy might be performed. The second procedure was used. The patient was not in the extreme lithotomy position so often used for forceps operations, as it places the soft tissues of the outlet under considerable tension and tearing is more likely to occur. Instead, the Sloan stirrups were low and inclined forward, allowing the buttocks to overhang the edge of the table slightly and leaving the outlet tissues under no tension.

With the DeLee modification of a Simpson instrument a cephalic-forceps application was made. Care was taken not to include in the grip of the forceps the loop of cord which encircled the neck. Trial traction was made after locking. When the fetal heart was auscultated it was found that the rate was only slightly decreased. With a sponge between the handles to prevent excessive compression on the head, I made traction leisurely, attempting to follow the uterine contractions in the gradual increase to maximal force and the less gradual decrease. The fetal heart tones were auscultated between each traction which were spaced a minute apart. The anesthetic was nitrous oxid and oxygen with just enough ethylene to keep the patient quiet. Deep surgical anesthesia was neither necessary nor desirable. When the head bulged the perineum a generous medio-lateral episiotomy was performed. The skin and underlying tissue were cut with the first snip and the incision in the vaginal mucous membrane extended somewhat with the second. The incision should be deep enough so that extension by tearing will not occur; if it does, the effect of the prophylactic widening of the soft-tissue outlet is defeated in part. With the next traction the head was carefully pulled over the perineum, the left hand being used to lift with the forceps and the right hand

protecting the perineum through eight thicknesses of a sterile towel to avoid contamination of the glove. The birth weight was 7.5 pounds.

The placenta was expelled from the vagina after ten minutes and repair of the episiotomy wound was carried out. Deep interrupted sutures of No. 2 chromic catgut united the fascia and the vaginal incision was closed by a submucous suture of catgut. The cervix need not be inspected unless there is bleeding. The remainder of the closure was made with two layers of twenty-day chromic catgut, No. 2, and the skin closed with subcuticular silkworm sutures. A generous bite of tissue should be taken with the deep catgut sutures to insure good approximation.

The diagnosis of occiput-posterior presentation is usually relatively simple. It is frequently associated with premature rupture of the membranes and a long first stage of labor. Occiput-posterior presentation is always looked for when the membranes rupture prematurely, particularly if rupture occurs at the onset of labor. The first stage is not prolonged because of the dry labor in itself, but because of the substitution of an ill-fitting and poorly placed vertex for the normal dilating wedge. In my experience, if there is well-flexed occiput-anterior position or breech presentation, dry labor is not prolonged, as a rule. Abdominal palpation usually reveals the small parts prominently on one side or the other with the back to the opposite flank and the fetal heart tones heard best in that region. On rectal examination early in labor the external os is often found far posterior and drawn to the side of the pelvis occupied by the occiput. Patients with an occipito-posterior presentation frequently complain greatly of backache throughout labor. With the increase in cervical dilatation, the sutures and fontanels can often be palpated to corroborate the abdominal findings. Occasionally vaginal examination is necessary to determine accurately the position and presentation. With the head molded extremely, as is often the case, the most reliable information comes from palpation of an ear.

Until interference becomes necessary in the second stage of

labor, relief of pain, relaxation in the first stage, and waiting in the second stage are of first importance. The use of morphin and oil-ether-colonic analgesia greatly simplifies the handling of these cases. The inhibition of pain and the period of rest allows the patient to arrive in the second stage with less nervous shock, a reserve of physical strength, and fair relaxation of the cervix. Dilatation usually occurs much more quickly under this type of treatment.

The induction of colonic analgesia is not a routine measure. The average multipara is carried along with morphin-magnesium sulphate, if necessary, during the first stage. During the second stage the usual anesthetic is given. Occasionally for a multipara with a scarred and slowly dilating cervix synergistic analgesia is valuable. The patient who seems to derive the greatest relief from analgesia is the primipara with a primary occiput-posterior presentation, with or without premature rupture of the membranes. Labor is not only prolonged in the majority of such cases, but is more painful than in the average case.

The few necessary drugs are easily obtained and carried. Sterile and chemically pure magnesium sulphate (25 per cent solution) can be secured in 2-c.c. ampules with or without morphin. The latter seems preferable, as morphin is usually given but once, whereas the magnesium sulphate may be repeated two or three times. The morphin is dissolved in 1 c.c. of sterile water and added to the contents of the ampule in the syringe just prior to injection. Triturate tablets of $\frac{1}{4}$ to $\frac{1}{6}$ grain of morphin should be available for each case.

The solution for rectal instillation is made up of 20 grains of quinin hydrobromid dissolved in 2 or 3 drams of 95 per cent alcohol, to which is added 2.5 ounces of ether, and the mixture made up to 4 ounces with olive oil or heavy liquid petrolatum. This, together with another 2 ounces of the olive-oil vehicle, is warmed to body temperature.

Quinin (alkaloid) may be used, but the hydrobromid of quinin is more easily soluble in alcohol and hence more satisfactory. This is usually made up in powders of 10 grains each. Two of these are added to the first instillation, and should

repetition be necessary, one powder of 10 grains is sufficient for the second instillation. Two or three drams of 95 per cent alcohol are needed to dissolve the quinin prior to mixing it with the ether and oil.

A $\frac{1}{4}$ -pound can of anesthetic ether is usually sufficient for each case. Two and a half ounces are used for the instillation, and the remainder can be used at the time of delivery, if needed. Olive oil or heavy liquid petrolatum is used as the vehicle, about 4 ounces for the average patient. Vaseline is used to protect the area around the anus.

The necessary apparatus is simple, consisting of a 5-ounce glass or porcelain funnel to which is attached 20 inches of rubber tubing connected to a No. 20 French catheter by means of a glass union. An artery clamp is used as a stop. For injecting the morphin-magnesium sulphate solution a 5-c.c. syringe with a long intramuscular needle is used. An ordinary hypodermic set is inadequate.

When labor has definitely begun, the patient is given an enema of soap-suds and injections of tap-water until the return is clear. It is important to have the rectum and lower colon clean, since much of the efficiency of the instillation depends on this. If eight hours have elapsed since the first enema, another should be given before ether is instilled into the colon.

It is important not to begin the injections too early, as the pains may thus be stopped. As soon as contractions are strong and occur every three or five minutes, and last from thirty to forty-five seconds, dilatation having reached 2 to 4 cm., and the patient complains of pain, $\frac{1}{6}$ or $\frac{1}{4}$ grain of morphin in 2 c.c. of magnesium sulphate is injected deep into the gluteal or deltoid muscle. Half an hour later 2 c.c. of magnesium sulphate is given without morphin.

The patient is made comfortable, the room darkened, and noise excluded. If a good sedative effect follows these injections, instillation into the colon is withheld until the action is nearly worn off and the patient again complains of pain.

If there is no relief from the injection, the instillation of oil and ether may be given in fifty minutes. The patient is turned

on the left side with the buttocks slightly elevated and toward the edge of the bed. It is carefully explained to the patient that the purpose of the oil and ether is to relieve pain, and that success depends a great deal on her coöperation. She is told that she will no doubt feel like expelling the mixture, and to avoid this is asked to breathe through her mouth, contract the sphincter ani, and "squeeze up" when she has a pain. The area around the anus is smeared with vaselin in order to prevent a burning sensation, should a little of the mixture be expelled around the catheter. An ounce of warm olive oil is now run into the funnel, tubing, and catheter to exclude all air. The catheter is then clamped 20 to 25 cm. from the tip and inserted under guidance of the finger to avoid coiling in the rectum. Should coiling occur, the entire mixture will be retained in the rectum below the presenting part and will be much more likely to be expelled. Half of the ether mixture is now poured into the funnel and allowed to run slowly into the bowel in the intervals between three or four pains. The clamp is replaced during the pain, counterpressure made over the anus with a towel, and the patient told to "squeeze up." The clamp may be removed during the first pain to allow the escape of gas which, if retained, would increase the desire to empty the bowel. It is for this reason that only half of the mixture is poured into the funnel, for were the funnel full some would be lost. When the catheter is once inserted it must be held in place so that it will not slip out.

As the last of the ether mixture is leaving the funnel one ounce of warm olive oil is added and the fluid level allowed to run down until the meniscus appears in the glass union; the clamp is applied and the pinched catheter allowed to remain in place through a few pains, counterpressure being made over the anus during a pain. After the catheter has been slowly withdrawn between pains, counterpressure is again maintained through another pain. At this time another intramuscular injection of 2 c.c. of magnesium sulphate is given. The patient then may lie in any position she chooses and is watched. No vaginal or rectal examinations are made for at least an hour.

One should not be misled by the quiet appearance of the patient, as the pains are coming at regular intervals. Their intensity, frequency, and duration should be ascertained by palpation of the abdomen.

Infrequently it becomes necessary to repeat the instillation; this should not be done with less than a two-and-a-half-hour interval. The effect of the initial olive-oil-ether mixture is allowed to wear off, and when the patient again complains of pain, a mixture of 2 ounces of ether and 2 ounces of olive oil containing 10 grains of quinin is instilled with the same technic and followed by the intramuscular injection of magnesium sulphate. Morphin is not given before the second instillation.

In the second stage time should be given for the head to be molded naturally. Good molding alone may mean the difference between a relatively simple maneuver, as in this instance, and a difficult, bruising forceps rotation and mid-forceps delivery. I do not think an arbitrary time can be set for interference in this or any other obstetric condition.

When manual rotation fails or forceps rotation is difficult it is always well to investigate the position of the posterior shoulder. As long as the promontory prevents it from following the head in its rotation the movement will be difficult to secure, and it will be still more difficult to retain the occiput in the anterior position. Occasionally the occiput will rotate to the sacral hollow and be directly posterior. Should this occur and descent continue, it is often preferable to deliver it as an occiput than to accomplish a difficult rotation.

The double application of forceps (Scanzoni method) may be used to effect rotation, but considerable skill and judgment are required in its accomplishment. Great injury to the maternal soft parts has been done with this method in unpractised hands. It certainly should not be employed until repeated attempts with the manual and Pomeroy rotation have failed.

Podalic version was a possible procedure in this case, as relatively little liquor amnii had been lost, but it also should be reserved in case of failure of the simple procedures. As a rule,

it is contraindicated after twenty hours of labor with ruptured membranes. The lower uterine segment is then considerably thinned out and rupture of the uterus has occurred under similar circumstances.

Occasionally the occiput can be rotated to the transverse diameter and no farther, or this occurs naturally, causing a condition known as deep transverse arrest. Forceps may be needed with the head in this position. If it is difficult to maintain the transverse position, the posterior blade of the forceps is applied first, regardless of which blade it may be. With this in place over the posterior mastoid process of the babe, the position remains fixed while the other blade is adjusted over the opposite (anterior) malar bone. Gentle traction will sometimes cause rotation to occur inside the blades. If not, traction will often affect it and the blades can be readjusted from time to time toward the usual cephalic application. The Kelland forceps may be of value in this type of case.

UNUSUAL UROLOGIC CASES

BENJAMIN H. HAGER AND WILLIAM F. BRAASCH

A REVIEW of the advances in urography during the last decade reveals two important facts: urologists have become more cognizant of the significance of the less conspicuous deformities or abnormalities in outline of the urogram, and they have learned to recognize the great variation in the appearance of the normal urogram. The first of these observations is particularly significant in the recognition of early renal tuberculosis and malignancy in which the other cystoscopic data may not be of much consequence. The classical examples of urograms depicting various urologic lesions are well known and need no consideration here. We shall, however, review the diagnostic difficulties encountered in a group of unusual cases, in some of which there was a discrepancy in the interpretation of the urograms and the observations at operation or necropsy; we shall emphasize further the importance of considering as corroborative evidence all available cystoscopic data and the history and objective symptoms before attempting to identify atypical urograms.

REPORT OF CASES

Case 1.—A physician aged forty-five, whose family and personal history were essentially negative, came to the Clinic with a history of recurring attacks of distress in the upper part of the abdomen not associated with food intake. The pain was more severe on the right side than on the left. Left renal colic with microscopic hematuria had occurred in July, 1926, and fluoroscopic examination at that time disclosed a large shadow on the right side which was thought to be renal stone. Another attack of colic occurred in January, 1927, although there were no recurrent symptoms.

The systolic blood pressure was 115 and the diastolic 78. There was a dense shadow in the right renal area (Fig. 239). Cystoscopy showed the bladder to be normal, urine was clear from both sides. Indigocarmin was given and there was concentration, graded 4, from each ureter. A specimen from the right ureter contained a few pus cells; a specimen from the left was negative

microscopically. A pyelogram of the right side (Fig. 240) showed what appeared to be a stone, 2.5 by 1 cm., at the tip of one of the minor calices of the superior calix. It was, however, difficult to reconcile this type of stone with acute colic, and the probability of gallstones was considered. A cholecystogram was negative. Exploration of the right kidney was performed, and a stone was found in the cortex of the upper pole.

In this case it was difficult to distinguish between extrarenal shadows and pseudocortical stones. True cortical stones prob-

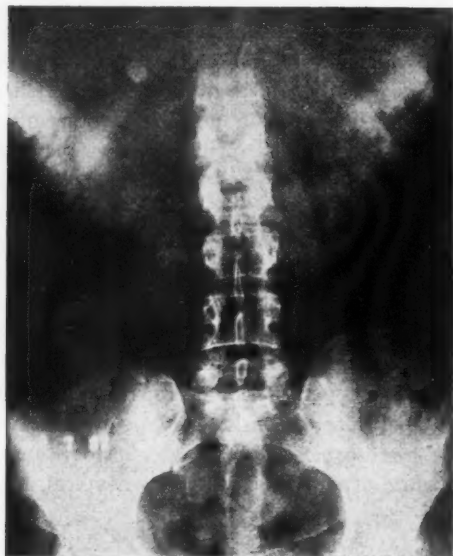


Fig. 239.—Dense shadow in right renal area over twelfth rib.

ably never occur. There are two varieties of shadows, however, in the renal parenchyma: those which result from deposition of calcium, as in renal tuberculosis, hypernephroma, and pyogenic abscess which has undergone resolution with calcification, and those caused by renal stones which may be described as pseudocortical and are always seen just distal to the minor calices. The second variety originates in the tips of the minor calices, and through a process of inflammatory reaction becomes

walled off and encysted, and in time becomes separated from the other calices by scar tissue. This is the variety of so-called cortical stone often seen in routine pyelography and which is well illustrated in this case. As would be expected from the anatomy of the kidney, the stones always appear distal to the minor calices and not laterally. Such stones may be lodged in



Fig. 240.—Right pyelogram with original shadow just distal to the minor calices of the upper major calix.

cicatricial tissue not unlike a cyst. In this case it would seem from the pyelogram that a minute sinus connected with the pelvic lumen was present. There is no evidence of deformity in the calices or pelvis. It is difficult to explain the cause of pain by increase in intrapelvic pressure.

Case 2.—A man aged fifty-five had had three attacks of pain two and a half years, two years, and ten days previous to examination. In the first two attacks the pain seemed to start in the left hip, but the severe pain radiated between the right groin and loin; it lasted for from ten to twelve hours.

The third attack was similar, but started in the right groin and radiated to the right testicle. Gonorrheal infection had occurred twenty years before.

The patient was obese. The systolic blood pressure was 160 and the diastolic 80. The urine contained pus, graded 2 (25 cells). The combined intravenous phenolsulphonephthalein return was 60 per cent; urea was 20 mg. for each 100 c.c. of blood; the Wassermann test on the blood was negative. Roentgenogram of the kidneys, ureters, and bladder showed a shadow on the left side opposite the second lumbar vertebra (Fig. 241). Cystoscopic ex-



Fig. 241.—Indefinite shadow in left renal area.

amination revealed a normal bladder with clear urine from both sides. Indigo-carmin was given; there was normal concentration of dye from both meatuses. Both ureteral specimens were microscopically negative. A pyelogram was made and the original shadow appeared to be obscured by the outline of the pyelogram. A diagnosis of left renal calculus was made (Fig. 242).

In view of the subjective symptoms with pain chiefly referable to the right renal area we were somewhat in doubt as to the correct interpretation of the pyelogram. It was therefore decided to make a pyelogram with the patient in the lateral position (Figs. 243, 244). This was done, and the



Fig. 242.—Left pyelogram with inclusion of original shadow.

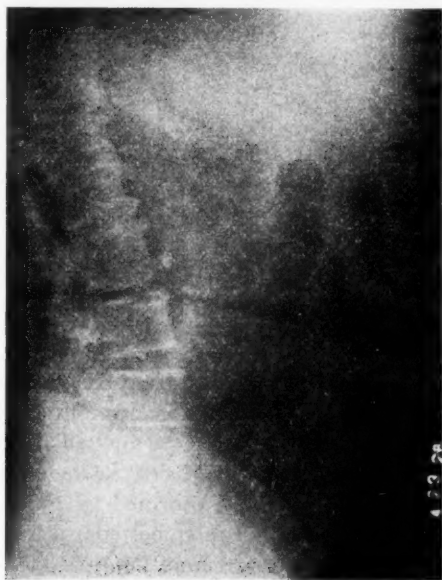


Fig. 243.—Kidneys, ureters, and bladder with patient in lateral position, showing original shadow opposite third lumbar vertebra.

shadow has again been interpreted as being within the renal pelvis. Operation was performed, and a stone, 11 by 9 by 5 mm., was removed from the left renal pelvis.

This case is of interest because it represents one of those rare conditions in which the lesion is opposite the side which manifests subjective symptoms. While the subject of renorenalis



Fig. 244.—Left pyelogram with patient in lateral position, showing inclusion of original shadow.

reflex is still a moot one, it is, nevertheless, true that occasionally a case, particularly one of lithiasis, may be explained by this phenomenon. It further illustrates the advisability of resorting to roentgenograms made with the patient in the lateral position when the shadow in question is obscured by the outline of a normal pyelogram made in the anteroposterior plane. The possibility of a stone having passed from the right kidney has not

been excluded. Cholecystography may be of much value in excluding doubtful shadows in the right renal area, particularly if the outline of the gallbladder is normal. However, the lateral pyelogram may be more accurate when the cholecystogram seems to include the doubtful shadow.

Case 3.—A man aged thirty-four had had kidney trouble for eighteen months. A specimen of urine had been sent to a life insurance company eighteen months previously. The patient was rejected for insurance because

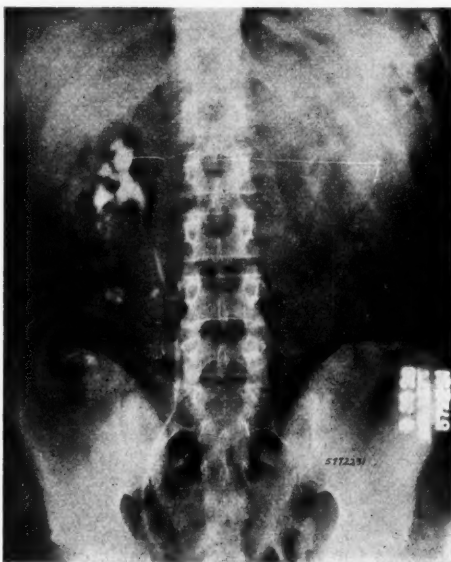


Fig. 245.—Cortical necrosis with multiple calcareous deposits over lower major calix suggestive of right renal tuberculosis.

of pyuria; there were no urinary symptoms. He had been sending specimens of urine to the insurance company since he was twenty-one years of age, and all the other examinations had been reported negative.

The patient was well developed and well nourished. The systolic blood pressure was 134 and the diastolic 90. Urinalysis showed pus, graded 3. Combined intravenous phenolsulphonephthalein was 75 per cent. The Wassermann test on the blood was negative. Roentgenogram of kidneys, ureters, and bladder showed multiple shadows in the right renal area. Cystoscopic examination revealed a normal bladder with clear urine spurting from

both meatuses. The ureters were catheterized, and differential functional tests were negative. A specimen from the right kidney showed pus, graded 2; that from the left was negative. A right pyelogram (Fig. 245) was made, and right renal tuberculosis with calcification of the lower pole was diagnosed. Specimens were obtained from both kidneys for guinea-pig inoculation, and subsequently both guinea-pigs were reported normal.

Right nephrectomy was performed. Tuberculosis was not found. There was extensive chronic nephritis and multiple hemorrhagic degenerating cysts, the largest 2 cm. in the lower pole and the smallest 1 cm. in the upper pole, also a small papillary adenoma, 4 mm. in diameter, and a single stone, 6 by 3 by 2 mm. Half of the kidney was destroyed.

This case portrays the difficulties in the differential diagnosis of calcareous pyelonephritis and tuberculosis with areas of calcification in the parenchyma adjacent to the minor calices. Even though there was nothing in the history indicative of tuberculosis and the ureteral specimens were both negative on guinea-pig inoculation, nevertheless, unilateral infection with the characteristic irregularities in the outline of the pyelogram, together with the pseudocortical calcareous deposits, is much more typical of a tuberculous process than of true lithiasis. Such pyelograms would be pathognomonic of tuberculosis in most cases. The normal outline of the ureter would, of course, have been unusual with tuberculosis. Another interesting feature of this case is the fact that the patient was without objective symptoms, and the first evidence of disease was detected by the physician who examined him for life insurance. It is remarkable that so many cases of genito-urinary disease are first recognized or suspected at the time of application for life insurance, a point which emphasizes the importance of complete general examinations yearly.

Case 4.—A man aged forty-five came to the Clinic because of nocturia, frequency, and urgency for the last six months. He had had pneumonia and influenza in 1918. Appendectomy had been performed in 1910. Six weeks before examination hematuria and severe pain referable to the left side had appeared.

General examination showed marked rigidity and tenderness over the left anterior wall and left posterior area. The systolic blood pressure was 120 and the diastolic 70. Urinalysis showed pus, graded 4, and leukocytes numbered 12,600. The blood urea was 34 mg. for each 100 c.c. Roentgenogram of kidneys, ureters, and bladder was negative. Cystoscopic examina-

tion showed tuberculous inflammation of the bladder. Indigocarmin was given and there was concentration, graded 3, from the right ureter and no return from the left. The left ureter was catheterized and a pyelogram made. Left renal tuberculosis was diagnosed (Fig. 246).

Left nephrectomy was performed. Severe pyonephrosis with practically complete destruction of the kidney was found.



Fig. 246.—Inflammatory type of pyelogram with cicatricial contraction of pelvis and marked dilatation of minor calices. Cicatricial elongation of upper major calix. Tuberculous pyonephrosis.

This unusual pyelogram in a case of tuberculous pyelonephrosis might easily confuse the condition with chronic atrophic pyelonephritis. Rarely a similar deformity is noted with neoplasm. It is most unusual to find such extensive tuberculosis present with so little involvement of the pelvis and ureters.

Case 5.—A woman aged forty-two came to the Clinic complaining of stomach trouble of eight years' duration. Appendectomy had been performed twenty years previously, uterine suspension eight years previously, and cholecystectomy in 1925. She became nauseated after eating sweet food and was unable to eat fat. Sharp abdominal pains occurred after eating. She was weak, exhausted, and dyspneic.

A tender mass was palpated in the right upper quadrant which felt like a ptosed kidney. Examination of the thyroid gland disclosed some evidence of hyperthyroidism, and it seemed advisable to perform thyroidectomy fol-



Fig. 247.—Bizarre pyelogram with dilatation of major calices and effacement of minor calices and an irregular filling defect of lower calix suggestive of cortical necrosis.

lowing investigation of the urinary tract. The systolic blood pressure was 110 and the diastolic 80. Urinalysis was negative except for an occasional pus cell. The combined intravenous phenolsulphonephthalein return was 60 per cent. Roentgenogram of kidneys, ureters, and bladder was negative. Cystoscopic examination revealed a normal bladder. Indigocarmin was given and there was good concentration from both sides. Both ureters were catheterized and a specimen from the right showed pus, graded 1 (20 cells); a specimen from the left was negative. The differential test with phenolsulphonephthalein showed 4 per cent from the right and 25 per cent from the left. A pyelogram (Fig. 247) suggested tuberculosis, although pyogenic

infection was not excluded. The ureteral specimens were both negative for acid-fast bacilli.

While the patient was in the hospital catheterized specimens from the bladder were stained for acid-fast bacilli, but all were negative except one, and that was doubtful. However, on the basis of the unilateral infection with suspicious deformities in the pyelogram suggestive of tuberculosis, right nephrectomy was performed. Adenocarcinoma of the kidney with multiple areas of necrosis was found.

Although the appearance in the outline of the pyelogram in this case is not identical with that of the preceding case there is still a strong resemblance to the deformity of the pyelographic outline. Deformity of the pelvis occurring with the alveolar type of carcinoma differs from that in hypernephroma in that it is usually an abbreviation and obliteration rather than elongation, as occurs with the latter. The absence of any dilatation in the ureter would be unusual with tuberculosis. The pelvic outline otherwise, however, would certainly be suggestive of it.

Case 6.—A single woman aged twenty-nine came to the Clinic because of hematuria. For the last two years she had felt distress in the right side of the abdomen which she had attributed to the gallbladder. During the last two months the distress had become more severe, and one week before examination there had been acute exacerbation of pain with hematuria and clots. This recurred three days later.

Urinalysis showed red blood cells, graded 3. The combined intravenous phenolsulphonephthalein return was 50 per cent. Cystoscopic examination revealed hemorrhagic urine spurting from the right meatus. Both ureters were catheterized and a differential functional test and right pyelogram made. Specimens from the ureters were negative except for the red cells in the specimen from the right. The differential functional test showed normal function of both kidneys. The right pyelogram (Fig. 248) was negative except for a small spicule of elongation extending from the lower major calix, together with an indefinite filling defect in the lower major calix probably from blood clot. Two other pyelograms (interval of a week) showed the same defect.

In view of the subjective history and the pyelographic data exploration of the right kidney and nephrectomy was performed. On the anterior surface of the kidney was a tumor about 2.5 cm. in diameter which extended down into the kidney and also projected above the surface of the kidney about 0.5 cm. Grossly the tumor resembled hypernephroma, even though it was in an unusual position. On microscopic examination the tumor proved to be a lipoma, which extended down through the kidney to the pelvis.

This case represents the importance of recognizing the less conspicuous deformities appearing in the outline of the pyelogram and emphasizes the importance of careful analysis of subjective and objective data in order that the correct interpretation of the pyelogram may be of corroborative evidence. The appearance of the pyelogram might be confused with one showing

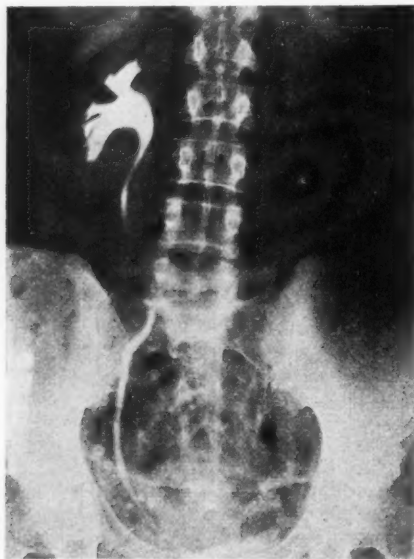


Fig. 248.—Normal pyelogram except for some suggestion of filling defect in lower major calyx as a result of blood clot with a spicule extending from lower major calyx suggestive of early neoplasm.

cicatricial elongation of the minor calices. The case might thus be mistaken for one of so-called essential hematuria, and treated accordingly. It is true, however, that the character of the hematuria is somewhat different from that observed with essential hematuria.

Case 7.—A man aged forty-six had always enjoyed good health aside from nervousness. He came to the Clinic because of attacks of pain in left upper abdominal quadrant of eighteen years' duration. He had had typhoid

fever followed by a rectal abscess about twenty-five years previously. The first attack of pain had come on eighteen years previously while he was walking. Several other attacks had occurred. The pain came suddenly, but increased in severity, lasting about twenty or thirty minutes, and disappeared as suddenly. There was slight residual soreness at the site of the pain for several hours. Attacks were aggravated by stress and strain and were relieved by rest.

The systolic blood pressure was 126 and the diastolic 78. Examination of stools was negative for parasites or ova. Urinalysis showed an occasional pus cell on several examinations. The combined intravenous phenolsulphone-



Fig. 249.—Chronic inflammatory changes with necrosis of the calices. Dilatation of the upper portion of the ureter with ureteral stricture below (renal tuberculosis).

phthalein return was 60 per cent. The blood Wassermann test was negative. Roentgenograms of the kidneys, ureters, bladder, and colon were negative.

Cystoscopic examination revealed slight cicatricial posterior urethritis and slight inflammation of the trigone. Both ureteral meatuses appeared normal. Indigocarmine was given and there was concentration, graded 4, from the right ureter, and concentration, graded 3, from the left. The left ureter

was catheterized on two occasions and specimens for guinea-pig inoculation obtained; these showed pus, graded 1 (8 cells). A left pyelogram was made (Fig. 249). There was no evidence of tuberculosis in the genitalia and there were no vesical symptoms. The two guinea-pigs inoculated with urine from the left ureter both reacted positively for tuberculosis. Left nephrectomy was performed. The pathologist reported multiple tuberculous pockets and destruction of about three-fourths of the kidney.

The irregularity in the outline of the pyelogram is typical of cortical necrosis and cicatrization occurring with chronic renal tuberculosis. A high degree of resistance or immunity is displayed in this case, as there was no evidence of tuberculosis in the genitalia or in the bladder; apparently the process was of long duration, possibly eighteen years. The dilatation of the upper portion of the ureter merging with the lumen of the renal pelvis is also suggestive of renal tuberculosis. There is apparently a stricture in the upper third of the ureter just below the ureteropelvic juncture and a filling defect in the ureter just below the stricture. The possibility of an element of spasm has not been excluded.

Case 8.—A man aged sixty-two came to the Clinic because of hematuria of sudden onset four months previously. Slight paralysis of the left leg had been noticed two years before admission. Blood had appeared at the beginning of micturition and cleared up. There was no pain or urinary symptoms. Four days before examination hematuria recurred, with urgency and frequency and considerable difficulty in voiding.

General examination showed an obese man with blood pressure of 158 systolic and 100 diastolic. A large fixed hard nodular mass was felt in the right hypochondrium. Urinalysis showed red blood cells, graded 5, and pus cells, graded 3. The blood urea was 36. The Wassermann test on the blood was negative. Roentgenogram of kidneys, ureters, and bladder was negative. Cystoscopic examination showed a normal bladder with slight trabeculation. Both ureters were catheterized without obstruction; 35 c.c. of residual urine was withdrawn from the pelvis of the left kidney. The differential functional test with phenolsulphonephthalein showed a return of 4 per cent from the right and 25 per cent from the left. The ureteral specimens were both negative. A right pyelogram (Fig. 250) showed some elongation and flattening of the lower calices. Exploration of the right kidney was performed. A large tumor of the right kidney was found extending from the diaphragm to the brim of the pelvis; it was irregular in outline and adherent to the perirenal fat. The pathologist reported hypernephroma, 14 by 9 cm., and destruction of about three-fourths of the kidney.

This extraordinarily large tumor was entirely lacking in the characteristic marked distortion and elongation of the calices so frequently seen with hypernephroma. The deformity occurring with hypernephroma is variable, depending on the site of the

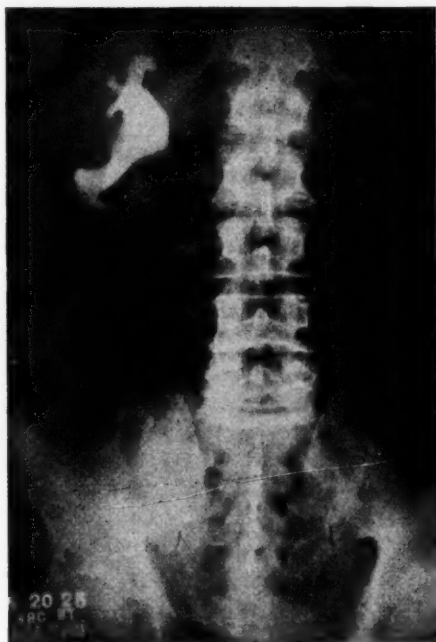


Fig. 250.—Bizarre type of pyelogram with marked dilatation and clubbing of upper and lower major calices.

growth and whether one or more of the calices are involved. However, deformity of this kind might occur in polycystic kidney, and in order to exclude this it would be necessary to make a pyelogram of the other side.

Case 9.—A woman aged forty-two came to the Clinic because of pleurisy, cough, and hematuria of one year's duration. She had never been robust; she had always been underweight, and suffered from migraine. One year previously a severe cold was followed by pleuritic pains in the right side of

the chest, some fever, and hematuria without pain or urinary symptoms. The hematuria had persisted intermittently during the last year. Two months after the onset severe pain had occurred in the left renal area, radiating to the groin and legs. The hematuria had occurred two days before admission.

General examination showed the patient to be undernourished and poorly developed. The systolic blood pressure was 104 and the diastolic 75. The left kidney was palpable. The urine contained blood, graded 4; it was negative for acid-fast bacilli. Roentgenogram of kidneys, ureters, and bladder was negative. The blood urea was 20. Cystoscopic examination

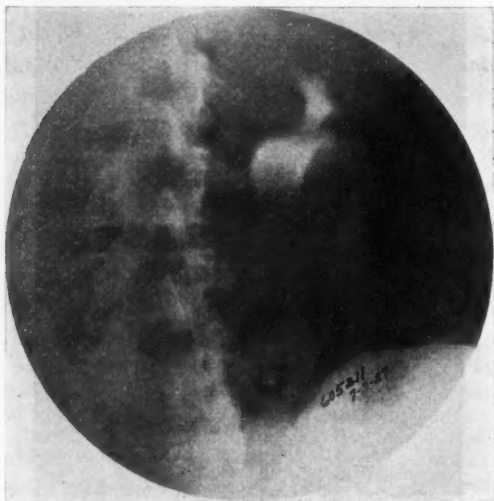


Fig. 251.—Bizarre pyelogram as a result of incomplete distention. Some suggestion of distortion as a result of catheter being pushed in middle major calix.

showed a normal bladder with clear urine from both sides. Both ureters were catheterized and specimens obtained for guinea-pig inoculation. The function of both kidneys was normal. A left pyelogram (Fig. 251) was made. The pelvis and calices were incompletely filled. The upper portion of the ureter was distorted and angulated, giving the impression that the ureteral catheter had been inserted into the tip of the middle major calix. The lower two-thirds of the ureter appeared dilated. Another pyelogram in which the pelvis and calices were completely filled (Fig. 252) showed deformity characteristic of neoplasm.

At exploration carcinoma of the left kidney involving the lower pole, which was about twice normal size, was found. Figure 251 is an example of artefacts occurring as a result of insufficient distention of the pelvis and calices and illustrates the difficulty in the correct interpretation. Figure 252,



Fig. 252.—Pyelogram with pelvis and calices completely filled. Characteristic elongation of calix indicative of neoplasm.

made four days later, in which the pelvis and calices are completely distended, presented the picture characteristic of renal neoplasm. The hook-shaped narrowing of the lower calix is typical of hypernephroma.

Case 10.—A woman aged thirty-three came to the Clinic because of weakness and menorrhagia. She had been treated for anemia since the age of seventeen, and had complained of general weakness and a tired feeling since she was a girl.

A mass was palpable in the right side of the abdomen. The systolic blood pressure was 134 and the diastolic 116. The urine was normal microscopically. Roentgenogram of kidneys, ureters, and bladder showed a large calcified shadow in the right renal area (Fig. 253). Cystoscopic examination was negative. A right pyelogram (Fig. 254) showed the pelvis incompletely filled with the lower calix extending below the shadow and deformed. The



Fig. 253.—Calcified shadow in right renal area.



Fig. 254.—Marked distortion as a result of encroachment of cyst on pelvis.

shadow encroached on the lateral border of the pelvis. The cyst was a simple cyst, and should not be confused with polycystic kidney. Simple cysts and cysts of polycystic kidney rarely undergo calcification.

At operation chronic nephritis and cyst of the cortex, 7 by 5 by 5 cm., partially filled with a gelatinous-like substance, were found. The walls of the cyst were undergoing calcareous degeneration. Two-fifths of the kidney was destroyed.

Case 11.—A single woman aged sixty came to the Clinic because of constipation and a "lump in the throat."

The general examination was negative except for a nodular mass in the right upper abdominal quadrant which appeared to move on respiration.



Fig. 255.—Huge shadow in right renal area.

The urine was normal. The combined intravenous phenolsulphonephthalein return was 45 per cent. The Wassermann test on the blood was negative. Roentgenogram of kidneys, ureters, and bladder showed a dense calcified shadow extending from the tenth to the level of the fifth lumbar vertebra on the right (Fig. 255). Cystoscopic examination showed a normal bladder and clear urine from both meatuses. The right ureter was catheterized and the



Fig. 253.—Calcified shadow in right renal area.



Fig. 254.—Marked distortion as a result of encroachment of cyst on pelvis.

shadow encroached on the lateral border of the pelvis. The cyst was a simple cyst, and should not be confused with polycystic kidney. Simple cysts and cysts of polycystic kidney rarely undergo calcification.

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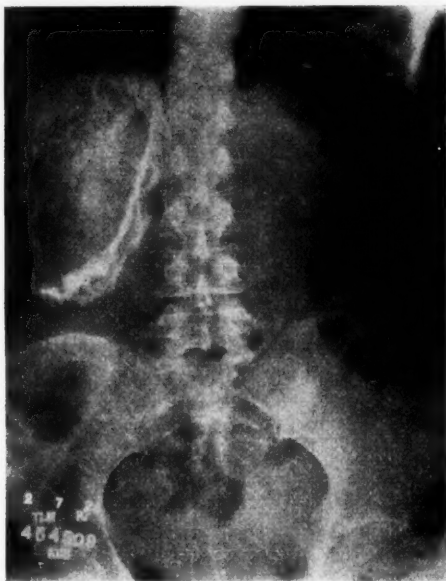


Fig. 255.—Huge shadow in right renal area.

The urine was normal. The combined intravenous phenolsulphonephthalein return was 45 per cent. The Wassermann test on the blood was negative. Roentgenogram of kidneys, ureters, and bladder showed a dense calcified shadow extending from the tenth to the level of the fifth lumbar vertebra on the right (Fig. 255). Cystoscopic examination showed a normal bladder and clear urine from both meatuses. The right ureter was catheterized and the

catheter could only be inserted a short distance. The pyelogram showed the shadow in question to be extrarenal (Fig. 256). The possibility of old perinephritis, or of calcified abscess of the liver was considered.



Fig. 256.—Shadow shown to be extrarenal. Downward displacement of kidney as a result of pressure from extrarenal mass is shown.

Case 12.—A man aged forty-three had sustained an injury to the kidney twenty-two years previously, following which hematuria had occurred. Influenza had occurred in 1920. He came to the Clinic because of pain in the jaws. He urinated from one to four times a night. Occasional burning and distress was felt in the right upper quadrant.

The general examination was negative. Urinalysis was negative. The combined intravenous phenolsulphonephthalein return was 65 per cent. Roentgenograms showed multiple large calcified areas in the region of the right kidney. Cystoscopic examination was negative. Both ureteral specimens were negative. A bilateral pyelogram was made, no medium appearing in the right urogram beyond the customary site of the ureteropelvic juncture, the left appeared normal (Fig. 257). The diagnosis of echinococcus cyst was not verified in this case, as the condition was not surgical, but the presumptive evidence suggested by the history and the appearance of the cystic calcification of the kidney seemed to warrant the assumption.



Fig. 257.—Bilateral pyelogram with occlusion of right kidney at or near ureteropelvic juncture apparently as a result of calcified echinococcus cyst of the kidney; the left pyelogram is normal. Note the distinct outline of mother and daughter cysts.

Case 13.—A man aged forty-one complained chiefly of difficulty of urination of eight years' duration. For eight years there had been hesitancy and difficulty in starting the stream. During the last five months he had had terminal dysuria accompanied by increased frequency and nocturia (ten to twenty times a night). There had never been complete retention, although the bladder did not feel empty.

The systolic blood pressure was 122 and the diastolic 78. Enlargement of the prostate was graded 2, and on palpation was more suggestive of prostatitis than of adenomatous enlargement. The urine contained pus, graded 2 (30 cells) and the blood urea was 16. The Wassermann test on the blood was negative. Roentgenogram of the kidneys, ureters, and bladder showed calcified areas in the region of the left kidney (Fig. 258). Cystoscopic examination revealed marked diffuse inflammation of the bladder with large bilateral intra-urethral prostatic enlargement. The right ureteral orifice was normal; the left was not seen. The right ureter was catheterized, and showed normal function and urine. Because of marked irritability and spasm of the bladder cystostomy was done. The patient was in the hospital for several weeks and during this time his general condition improved. Cystoscopic

examination before he left the Clinic showed that the prostate was smaller and that there was no evidence of an intra-urethral enlargement.

The patient died at home March 1, 1927, approximately four months after dismissal from the hospital. The necropsy report was sent to us. The left kidney was found attached to the hard mass in the left upper quadrant. The suprarenal gland was adherent to the upper part of the mass which was semilunar in shape, and running into its concave border were two tube-like, narrow strips of tissue, apparently continuations upward of the left ureter, which was considerably dilated, tortuous, and thickened. A probe could not be passed into the small branches from the ureter, nor from the ureter into



Fig. 258.—Multiple circular shadows in left renal area presumably a calcified renal hydatid and illustrating a mother cyst with several daughtercysts.

the bladder; the branches represented the renal pelvis. The original hard rounded mass was enclosed in a membranous structure which also covered what was believed to be the kidney. The renal cysts apparently were originally solitary or multilocular, subsequently becoming divided into several isolated cysts. The character of their walls indicated that they had been present for a long time. There was marked pyelonephritis in a greatly hypertrophied kidney. A hemolytic streptococcus was isolated from the heart's blood at necropsy. Although no reference is made to echinococcus cyst the appearance is suggestive of such a condition.

Case 14.—A man aged thirty-three came to the Clinic because of pain in the left costovertebral angle and hematuria. In 1926, four days after appendectomy had been performed, severe pain developed in the left costovertebral angle radiating to the genitalia and lasting four days. Stone in the kidney was suspected, but was not shown in the roentgenograms. Hematuria did not recur for eight months, although pyuria persisted. October 1 severe hematuria occurred, which lasted a week and was accompanied by costovertebral pain.

The patient was fairly well developed and well nourished. The systolic blood pressure was 121 and the diastolic 84. The specific gravity of the

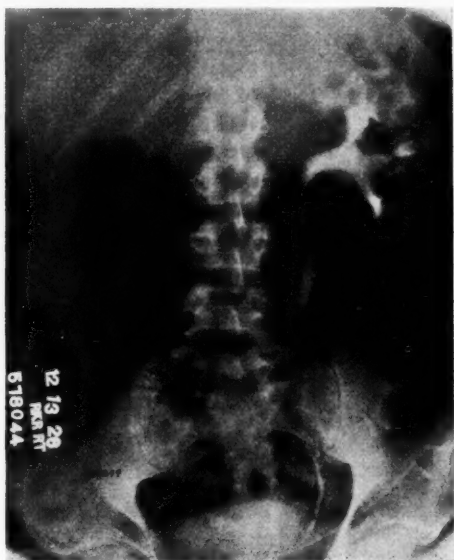


Fig. 259.—Bizarre type of pyelogram with huge major and minor calices suggestive of early polycystic kidney.

urine was 1.012. An occasional red blood cell, and pus, graded 3 to 4, were noted on several analyses. The combined intravenous phenolsulphonephthalein return was 50 per cent. Roentgenograms showed small shadows in the lower pole of both kidneys. Cystoscopic examination showed moderate stricture of the posterior urethra. The bladder appeared normal, with clear urine from the left meatus and turbid urine from the right. Both ureters were catheterized and guinea-pig inoculation was carried out. A specimen from the right ureter showed pus graded 3; from the left it was graded 1 (2 cells), and was graded 2 on a subsequent cystoscopic examination. The phenol-

sulphonaphthalein test showed a return of 10 per cent from the right ureter and 1 per cent from the left; there was no return from bladder.

A left pyelogram (Fig. 259) showed an unusual type of pelvis with large calices somewhat suggestive of polycystic kidney. On a second cystoscopic examination the differential functional test revealed a return of phenol-sulphonaphthalein of 5 per cent from the right ureter, a faint return from the left ureter, and no return from the bladder. A ureteral specimen at this time showed pus graded 3, from the right. A right pyelogram (Fig. 260) presented irregularities and deformities typical of polycystic kidney. Guinea-pig inoculations were negative for tuberculosis. A diagnosis was made of bilateral polycystic kidneys with pyelonephritis.



Fig. 260.—Right pyelogram showing characteristic outline of polycystic kidney.

This case of bilateral polycystic disease with pyelonephritis is of interest because of the absence of the customary subjective symptoms incident to the cystic degeneration of the kidneys and because of the marked variation in deformity of the outline of the two pyelograms, illustrating that if both kidneys are polycystic one may be much larger and renal parenchyma de-

creased as a result. Although both may produce deformities in the outline of the pyelogram typical of polycystic disease, one may show considerably more deformity than the other. Evidence of hypertension, urea retention, and reduction of combined intravenous phenolsulphonephthalein return together with palpable bilateral masses, so frequently seen in advanced cases of polycystic kidney, were not present in this case. While the hematuria can probably be explained as a sequela of the pyelonephritis, it may occur as a complication of polycystic kidney.



Fig. 261.—Left renal tuberculosis. Return of sufficient medium from the left pelvis and ureter to outline a small contracted irregular bladder. Regurgitation of vesical contents up the right ureter, dimly outlining the pelvis and calices.

Case 15.—A man aged twenty came to the Clinic because of frequency and burning on urination which had begun eleven months previously.

Urinalysis showed pyuria. The combined functional test showed a return of 70 per cent. The blood urea was 16 mg. Roentgenograms showed tuberculous arthritis of the right hip and evidence of tuberculosis of both apices. Kidneys, ureters, and bladder were normal. Bacilli of tuberculosis

were found in the urine. Cystoscopic examination revealed tuberculous cystitis. Both ureters were catheterized. The differential functional test was 20 per cent from the right kidney, 15 per cent from the left, and 4 per cent from the bladder. A specimen from the right kidney was negative, and that from the left kidney contained pus, graded 2, and bacilli of tuberculosis. Tuberculosis did not develop in guinea-pigs inoculated with urine from the right kidney. A pyelogram of the left kidney was characteristic of tuberculosis (Fig. 261).

Figure 261 illustrates renal tuberculosis with sufficient return of medium from the left pelvis and ureter to outline a small



Fig. 262.—Multiple shadows in region of bladder.

contracted irregular bladder, as well as regurgitation of the vesical contents up the right ureter, dimly outlining the pelvis and calices. The phenomenon of vesical regurgitation as a result of inflammatory changes in the bladder is clearly portrayed. The fact that regurgitation of vesical contents takes place under such conditions may explain the discrepancy in

diagnosis of so-called bilateral renal tuberculosis in which the symptoms disappear and the general health improves if the kidney which shows gross evidence of disease in the outline of the pyelogram is removed.

Case 16.—A man aged seventy-six came to the Clinic because of urinary trouble of four to five years' duration. The chief symptoms were burning and slight hesitancy in starting the stream. For the last three years there had been nocturia and rather marked frequency. A catheter had not been used.

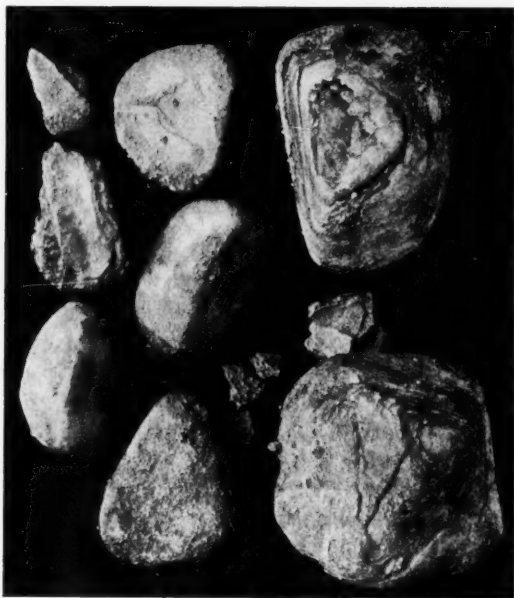


Fig. 263.—Stones removed from the bladder at operation.

The systolic blood pressure was 174 and the diastolic 92. Urinalysis revealed red blood cells, graded 1, and pus graded 3. The blood urea was 34 mg. for each 100 c.c. The Wassermann test on the blood was negative. Roentgenogram of kidneys, ureters, and bladder showed a large shadow over the area of the bladder. The prostate appeared enlarged by rectum. A diagnosis of benign hypertrophy of the prostate with multiple stones in the bladder was made. Three stones approximately 7.5 cm. in diameter and three smaller stones approximately 2.5 cm. in diameter were removed by

cystostomy (Figs. 262, 263). Slight intravesical enlargement of the prostate was noted.

Case 17.—A man aged sixty-two came to the Clinic because of urinary disturbances which had been present for ten or twelve years, gradually increasing in severity so that during the last five years he had been incapacitated. Frequency (from fifteen minutes to one hour by day, five or six times at night with urgency), slight incontinence, difficulty in starting stream and interruption of stream were complained of. Pain in the sacro-iliac region was not constant.

The systolic blood pressure was 138 and the diastolic 80. The tonsils were infected and the enlargement was graded 2. There was some tender-



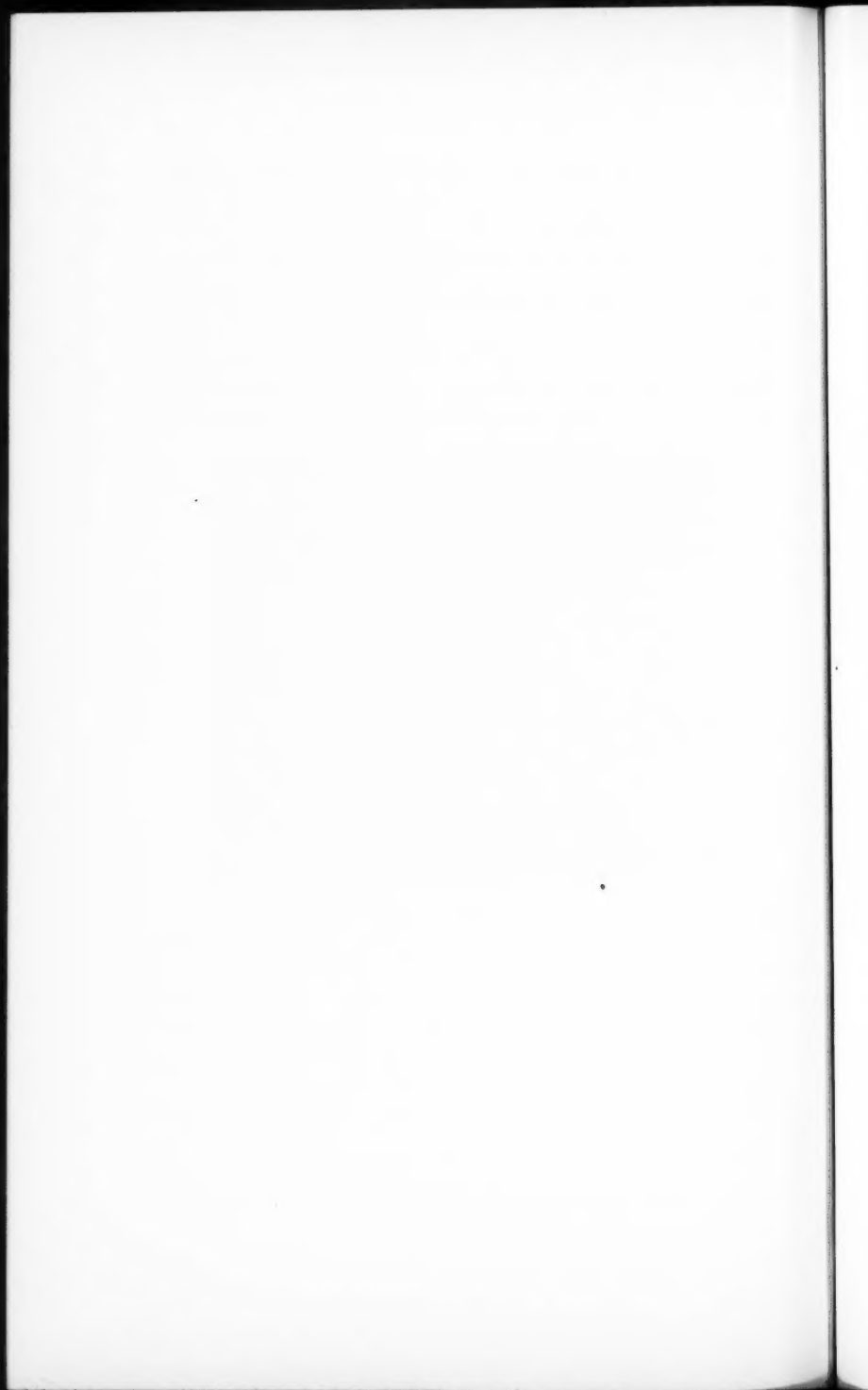
Fig. 264.—Multiple shadows in region of bladder and prostate. The smaller shadow was a stone in a diverticulum and the larger shadow a huge prostatic calculus.

ness in the lower left quadrant of the abdomen and a few palpable inguinal nodes. The prostate could not be definitely outlined by rectum, but appeared flat and spread out, with an irregular contour suggestive, although not typical, of carcinoma. The urine had a specific gravity of 1.021, the reaction was acid, and it contained red blood cells, graded 3, and pus, graded 4. The combined intravenous phenolsulphonephthalein return was 70 per cent. The blood urea was 34 mg. for each 100 c.c. and the Wassermann test on the blood was negative. Roentgenograms of the kidneys, ureters, and bladder revealed two large shadows over the area of the bladder.

A diagnosis was made of multiple large stones in the bladder, largest

8 by 5 cm., and of a smaller stone, 3 by 2 cm., in a diverticulum (Fig. 264). Cystostomy was performed with the removal of a single large stone from the diverticulum in the base of the bladder. The large triangular stone was in the prostate itself. It seemed advisable only to drain the bladder and diverticulum, and remove the large pyramidal prostatic stone later. The stone occupied exactly the same position as though it had been the hypertrophied lateral and median lobes of an adenomatous hypertrophied prostate gland.

Cases 16 and 17 illustrate huge shadows in the region of the bladder. They represent different pathologic conditions, even though there is a strong resemblance in the outline of the shadows in the original roentgenograms.



SOME SIDELIGHTS ON HYPERTENSION

LEONARD G. ROWNTREE

HYPERTENSION is an extremely familiar but poorly understood condition. We diagnose hypertension, treat hundreds of its victims, measure the blood pressure with considerable accuracy, determine its effects on various body processes, follow patients to recovery or death, and perform many necropsies in cases in which the disease is present, yet our knowledge of its etiology and pathogenesis is extremely scanty. In many respects our conception of this disease has progressed materially during the last twenty-five years. This has come about because of improvement in the methods of determining blood pressure and in our knowledge of this disease.

Although the blood pressure of animals was determined as early as 1727 by Hales, real knowledge of this subject began with the kymographic studies and the graphic forms of record introduced into physiology by Ludwig in 1847. Attempts to study blood pressure clinically were made by Vierordt, Marey, Basch, Riva-Rocci, Hill, and Allbutt, abroad, and in this country by Erlanger, Cook, Janeway, and many others. Most of our knowledge dates from the beginning of the present century. The sphygmomanometer has now come into general use throughout the world, so that the presence of hypertension is commonly recognized.

Because hypertension commonly occurs in nephritis and in association with arteriosclerosis the belief has become established that it is related to diseases of the kidney and to arteriosclerosis. A careful clinical analysis of many cases of this disease and, in recent years, the use of renal functional tests have served to dispel the idea that hypertension is, of necessity, due to either of these causes. We are forced to the conclusion

that hypertension may exist when the kidneys are apparently normal and when significant arteriosclerosis or atheroma is absent. It may exist as an independent disease of unknown origin, that is, it may run a course of weeks or months and then disappear, sometimes spontaneously. It may continue for years without appearing to do any actual harm, or it may be fulminating in character, bringing about the death of the patient within the course of months. The causes of death relate frequently to cardiac failure or decompensation, cerebral vascular accidents, renal insufficiency, and uremia, alone or in combination.

As already indicated, the cause of hypertension is not known. In health the blood pressure is maintained within normal limits and is subject to considerable change to meet the varying demands of the body. According to Janeway (1904) the factors which determine blood pressure are: (1) The energy of the heart, (2) the peripheral resistance, (3) the elasticity of the arterial wall, and (4) the volume of blood. Health demands perfect harmony between the vessels and vasomotor center and the heart. In hypertension this is disturbed. Neither the cause nor the mechanism of the disturbance has been definitely determined.

There is no dearth of theories on factors causing hypertension. They may be grouped as mechanical factors, including atheroma, sclerosis, capillary fibrosis, and chemical factors: pressor hormones derived from the glands of internal secretion such as the suprarenal and pituitary or other pressor substances, toxins from the kidney, toxic products from gastro-intestinal putrefaction, iso-amylamine, phenylethylamine, and parahydroxyphenylethylamine (Barger and Dale), or such substances as guanidine. The real cause of hypertension, however, still remains unknown.

In recent years the possible rôle of the sympathetic nervous system in hypertension has impressed me greatly, so much that I am inclined to believe that surgeons should take an active interest in the subject. Certainly, with the wide-spread prevalence of hypertension and the inadequacy of medical measures in a large proportion of cases, the possibilities of surgical treat-

ment should not be overlooked and the surgeon should retain a working acquaintance with the subject.

I wish to present a series of cases in which hypertension played a major part. These cases are selected with the idea of furnishing material for thought. They serve to emphasize the lack of knowledge concerning hypertension and to indicate the need of further investigation of this most important clinical problem.

Case 1. Hyperpiesia*; essential hypertension, sudden and prolonged remission of hypertension with fever.—A man of Jewish descent, aged fifty-five, came to the Clinic in December, 1923, with the complaint of headaches. He had had periodic headaches for many years, which, during the last five years, had become more frequent and were associated with vertigo. Peptone injections had been used in treating the migraine, with some relief.

The patient was short and stout. The systolic blood pressure was 238 and the diastolic 140; the pulse was 80. Examination of the urine and blood and the Wassermann test were negative. The blood urea was 28 mg. for each 100 c.c. Phenolsulphonephthalein excretion was 40 per cent in two hours. The retinal vessels showed moderate sclerosis with a few cotton-wool exudates of the hypertension type. Electrocardiogram showed inverted T-wave in Lead III. The patient was sent to the hospital. After two days' rest the systolic blood pressure was reduced to 150, the diastolic to 90; the water concentration tests showed maximal concentration of 1.016 and a water excretion of 1,300 c.c. in the first four hours. The patient was allowed to return home on a restricted regimen, including an intake of fluid of 1,500 c.c.

The patient returned to the Clinic in September, 1926. He had had many and varied treatments for hypertension. In July, 1926 the blood pressure suddenly and spontaneously dropped to normal, and a few days later there was a severe chill and rise of temperature. During the succeeding days he had severe chills lasting for half an hour. From that time until he came to the Clinic he had remained in bed. The blood pressure remained normal. At this time the systolic blood pressure was 130 and the diastolic 70. There was intermittent pyrexia every second or third day, and the temperature reached 101° F.; the pulse varied between 70 and 100. There were no signs of obvious infection. The test of hepatic function showed dye retention, graded 2. Prostatitis, graded 3, was present. Daily prostatic treatments and rectal irrigation were begun and medication with emetin hydrochlorid instituted. Under this regimen the temperature gradually subsided. A month later it had been reduced to normal, although there were occasional

* Because of misconceptions attending the use of the term "hypertension" Allbutt has introduced the terms "hyperpiesia" and "hyperpiesis." "Hyperpiesia has been used to fix the identity of the pathologic state which is free from any organic associations beyond cardiac hypertrophy and arterial vessels; the blood pressure is raised in this condition, that is to say, hyperpiesis is a sign of the disease hyperpiesia."

exacerbations of half a degree. The blood on second examination showed slight secondary anemia; the leukocytes numbered 8,200; there was nothing abnormal in the differential count. The electrocardiogram was negative. Roentgenograms of the chest and examination of the genito-urinary tract were negative. The phenolsulphonephthalein return was 45 per cent in two hours. The amounts of blood urea, creatinin, and plasma chlorids were normal. Cholecystograms were positive. Urinalysis was always negative.

This represents a well-defined case of hyperpiesia or essential hypertension with moderate vascular changes, as seen in the retinal vessels, and early myocardial degeneration. Pyrexia, apparently due to prostatic infection, persisted for approximately three months. During this time the blood pressure returned to normal and remained normal or slightly subnormal during the entire period of observation. There was no evidence to suggest that the infection had produced renal or cardiac insufficiency or any other deleterious effect on the body. It is not known whether or not the treatment of prostatitis was a factor in the disappearance of hypertension; the infection itself, or rest and other factors in the regimen adopted, may have played a part.

Case 2. Essential hypertension.—A man aged forty-four, a railroad conductor, first came to the Clinic in March, 1922. At that time he complained of headache and pain in his shoulders. For the last three years severe occipital headaches had been present which were generally worse toward evening; sometimes they were absent for periods of two weeks. He complained of pain over the right scapula, radiating down the arm and forearm to the second and third fingers, also of some weakness in the legs when walking, especially when going upstairs. He said that one sister had hypertension and one brother and one sister low blood pressure.

At general examination the systolic blood pressure was 212 and the diastolic 138, the pulse 96, and the temperature 98.6° F. The patient weighed 180 pounds. The transverse diameter of the heart was 14 cm. Ophthalmoscopic examination revealed irregularity of the caliber of the arteries and moderate arteriovenous compression. There was evidence of recent and old hemorrhage in the peripapillary region. Examination of the ears, nose, and throat was essentially negative. The specific gravity of the urine was 1.025; it combined albumin, graded 3, and occasional hyaline casts. The electrocardiogram showed inverted T-wave in Leads II and III and premature auricular contractions. The basal metabolic rate was +10. Blood urea was 40 mg. and creatinin 1.6 mg. for each 100 c.c. The phenolsulphonephthalein test showed 65 per cent return of the dye in two hours. The erythrocytes

numbered 4,740,000, the leukocytes 5,600. The water tests showed excretion of 950 c.c. in the first four hours. The neurologic diagnosis was headache of arteriosclerotic origin. The patient was given a low-calorie diet (60 gm. protein) and was advised to reduce his activities and to take more frequent vacations and periods of relaxation.

The patient returned in May, 1925, complaining of occipital headaches. The headaches had been less severe until the two months previously, when he noticed a dull occipital ache extending over the scalp. There was no complaint regarding the heart and kidneys. The patient weighed 162 pounds; the systolic blood pressure was 162, the diastolic 108, and there was moderate cardiac hypertrophy. Ophthalmoscopic examination showed mild fibrosis of the retinal arteries, but was otherwise negative. The phenolsulphonephthalein return was 60 per cent in two hours; the blood urea was 24 mg. for each 100 c.c. There was no albumin in the urine, but occasional hyaline casts were present. The patient was urged to continue his previous regimen with a further slight reduction in activity. He was allowed to continue work, but was advised to rest and relax as much as possible between periods of duty.

The patient came for the third time in April, 1926. He felt well. Headaches and slight dyspnea on exertion were the only complaints. The systolic blood pressure was 200, the diastolic 130; pulse was 80 and temperature 98° F. The electrocardiogram showed sinus rhythm and left ventricular preponderance. The phenolsulphonephthalein excretion was 50 per cent in two hours. There was no anemia. The blood urea was 31 mg. and creatinin 1.1 mg. for each 100 c.c. The maximal specific gravity of the urine was 1.022. He was allowed to return home without any further changes in his treatment.

The patient was next seen in April, 1927. The systolic blood pressure at this time was 220, the diastolic 135, the pulse was 82. He weighed 148 pounds. There was no particular complaint. The electrocardiogram was essentially negative. Hemoglobin was 85 per cent (Dare), and the erythrocytes numbered 4,820,000. The phenolsulphonephthalein excretion was 80 per cent in two hours. Urinalysis was negative. The maximal specific gravity of the urine was 1.026. The blood urea was 28 mg. and the creatinin 1.5 mg. for each 100 c.c. The second day, after rest in bed, the systolic blood pressure was 170, the diastolic 112. At the time of dismissal with moderate activity the systolic blood pressure was 145, the diastolic 85. The patient felt exceptionally well. He was allowed to continue work as a railroad conductor and was urged to continue living moderately.

There are several points of particular interest in this case. The patient was under observation at intervals for more than four years, during which the blood pressure became established at a lower level and the general condition was much improved. He had no symptoms at the end of the four years. When first seen the vascular system was apparently suffering some injury, as evidenced by retinal hemorrhage, inversion of the T-wave

in the electrocardiogram, and by the general symptoms which were distinctly troublesome. After a time the condition improved. T-wave negativity disappeared. The blood pressure subsided, so that at the time of the third visit it was not of much moment, and there were no symptoms. At the last visit there was evidence of elevation of the blood pressure, which quickly subsided after a few days' rest.

The point illustrated by this case is that in essential hypertension there are periods of decompensation with elevation of blood pressure and evidence of vascular injury which subside under a suitable regimen. It is important not to have too dogmatic an attitude on prognostic criteria during these periods; a number of patients are seen at the Mayo Clinic who have been restored almost completely to normal. The factors that cause these periods of decompensation or vascular injury are unknown, but there is a possibility that it might be intercurrent infection, such as influenza or upper respiratory infection. It is extremely important that in many cases of this type of disease compensation takes place to a remarkable degree. In fact, hypertension may progress by successive periods of acute exacerbation just like chronic nephritis. Knowledge of this fact leads to conservatism in passing judgment without adequate observation of the patient and of his disease.

Case 3. Malignant hypertension.*—A man aged thirty-three came to the Clinic November 10, 1924, complaining of blurring of vision and headache ascribed by his physicians to high blood pressure. The family history was unimportant, except that the mother died from apoplexy. The patient had had typhoid fever in 1903, acute rheumatic fever while in the army in 1917, influenza in 1918, and an attack of indigestion in 1919 which caused him to consult a physician. It was at this time that he was informed that he had high blood pressure (systolic 190). Subsequently the tonsils were removed. In 1920 he felt dazed and depressed for a period of five weeks, and his memory seemed faulty. Eight months before examination he began to suffer from occipital headaches; the pain radiated to the vertex and was accompanied by nausea and vomiting, which were worse before breakfast, but usually "wore off" by afternoon. This headache was almost continuous for eight

* This case was reported by Rowntree, L. G., and Adson A. W.: Bilateral lumbar sympathetic neurectomy in the treatment of malignant hypertension: report of a case, *Jour. Am. Med. Assn.*, 1925, lxxxv, 959-961.

months. In November, 1924 vision began to fail, and he noticed gradually increasing blind spots in each eye.

The patient was well nourished and powerfully built; the weight was 185 pounds (84 kg.). Six teeth were infected, and there were tonsillar tags on both sides. The peripheral vessels were moderately sclerosed and the heart slightly enlarged. The systolic blood pressure was 230, the diastolic 130. Neurologic examination showed nothing of importance. Ophthalmoscopic examination revealed slight edema of the disks, cotton-wool exudates, hemorrhage involving especially the left macular region, and general reduction in the size and caliber of the retinal arteries. Repeated urinalyses were negative except for slight albuminuria. The phenolsulphonophthalein output was 70 per cent in two hours, and the values for blood urea and creatinin were normal. The hemoglobin was 75 per cent (Dare); the erythrocytes numbered 4,400,000, and the leukocytes 5,200. The Wassermann test on two occasions was negative. Electrocardiogram and a roentgenogram of the chest showed no abnormality. The dilution and concentration tests of renal function showed variations in specific gravity of the urine from 1.006 to 1.024, or a slight reduction in dilution capacity. The salt test yielded normal results. The diagnosis was "early malignant hypertension."

Because of the patient's age and excellent physical condition, aside from the vascular involvement, the possibility of relief by abdominal sympathetic neurectomy was discussed with him. Even recognizing that the operation was, in a sense, entirely experimental, he evidenced great enthusiasm, stating that he was willing to undergo any procedure that offered hope of permanent or even temporary relief. During the three weeks of medical treatment in the hospital blood pressure continued high, the systolic being from 170 to 200 and the diastolic from 90 to 130, and he complained of marked blurring of vision, headache, and weakness.

In the operating room the systolic pressure was 255 and the diastolic 190. The blood pressure was followed and recorded during the operation.

The patient recovered without interruption; he was in bed for two weeks, and then was up and about the ward. He was given a diet of 2,200 calories with 50 gm. of protein. At first the subjective improvement was striking. The blood pressure level was distinctly lowered, at least for the two weeks following operation. The headaches, which had previously occasioned such great distress, entirely disappeared, and recurred only once during the first month and even then only for a brief period. Vision improved markedly; the blind spots decreased materially so that he read almost any print with comfort. No change was noted in volume or composition of the urine; certainly the efficiency of the kidney was in no way impaired.

While the patient was resuming activity the blood pressure gradually mounted. On one occasion headache and epigastric distress recurred for a day or so. The response to nitrates and to the hypertension baths was good, much better than before operation. A letter received four and a half months after the operation expressed great satisfaction in the subjective improvement. On only one occasion had he suffered from headache and epigastric distress. After six months he reported recurrence of hypertension (systolic blood pressure 220, diastolic 120), but he was otherwise in good health. He

lived for fifteen months, was free from all symptoms, and worked every day; however, hypertension persisted. Finally notice of his death was received, but all attempts to ascertain the cause of death and the nature of the final illness have failed.

The malignant form of hypertension affects persons in the prime of life, usually men who are active and who have attained success at the expense of their vascular systems. In some instances malignant hypertension develops from a benign form, while in others it is malignant almost from its inception. Approximately 10 per cent of the total number of cases of malignant hypertension treated on my hospital service are of the malignant type. The cause of the disease is unknown; the course is stormy and rapid; the prognosis is extremely grave, and medical treatment is entirely unsatisfactory.

The clinical signs and symptoms are: (1) Marked and continuous elevation of systolic blood pressure and disproportionately high diastolic pressure; (2) cerebral manifestations; excruciating dull headaches, intermittent or continuous in character, affecting, as a rule, the entire cranium, but centering especially in the occiput; insomnia; irritability and mental deterioration; changes in personality and, at times, apoplectic or epileptiform seizures; (3) loss of visual acuity secondary to neuroretinitis and following hypertensive changes in the retinal vessels, constriction, spasm, hemorrhage, and so forth; (4) gastrointestinal disturbances, especially epigastric discomfort, nausea, and vomiting; (5) cardiac changes, enlargement and, at times, dilatation with the accompanying symptoms; (6) involvement of the kidneys, nocturia, albuminuria, cylindruria and sometimes eventual renal insufficiency, and (7) asthenia, which may be the outstanding feature. So striking are the cerebral features that brain tumor is sometimes diagnosed. The extent to which cerebral, cardiac, and renal manifestations participate probably depends on the relative involvement of the vessels to these organs. Death results, in order of frequency, from cerebral vascular accident, from cardiac failure, and from renal insufficiency. The course of the disease is rarely longer than two years, during which the patient, as a rule, suffers intensely from

headache, visual disturbances, or manifestations of cardiorenal vascular disease, and is, for the most part, incapacitated for work. Keith and Wagener have emphasized the existence of a group in which the changes in the eye-grounds are distinctive of this disease prior to the onset of severe renal cardiac or cerebral manifestations.

In this case operation was partially successful at least. At the time of operation only the second, third, and fourth lumbar sympathetic ganglia were removed. It is desirable, of course, to go higher so as to extirpate the ganglia governing the splanchnic area and abdominal viscera.

The next three cases are instances of intermittent paroxysmal hypertension which are probably in the nature of generalized vascular crises. This is a particularly interesting group because it proves that marked hypertension can be induced through functional rather than organic changes in the vessels. They point to the important rôle of the sympathetic nervous system in affections of the vascular system.

Case 4. Paroxysmal hypertension with tumor of retroperitoneal nerve.*—

A woman aged thirty, a music teacher, came to the Clinic, June 2, 1926, complaining of attacks of dyspnea, occipital headache, tachycardia, and vomiting. For eight or ten years previously she had felt "run down," but had carried on her occupation. She had suffered from moderate constipation for six years, and the appendix had been removed three years previously. The paroxysmal attacks had commenced one and a half years before and had been increasing in frequency and severity; they had occurred every day or two for periods of from six to eight weeks; each one lasted from a half hour to three or four hours and was followed by severe prostration. Some blood had been brought up into the mouth, but the patient was not certain whether it was vomited or expectorated. Several infected teeth had been removed, and a "rest cure" had been followed for eight weeks with doubtful results.

The patient was of the asthenic type, undernourished, and somewhat pale. The tonsils had been cleanly removed. The heart and lungs were normal. The abdomen was normal except for the operative scar. The reflexes were normal. The pulse rate and temperature were normal; the systolic blood pressure was 130, the diastolic 82. The urinalysis, gastric analysis, blood Wassermann tests, electrocardiogram, and roentgenograms of the chest, sinuses, esophagus, stomach, and colon all were negative. The hemo-

* This case was discussed by C. H. Mayo, *Journal of American Medical Association*, 1927, lxxxix, 1047-1050.

globin was 52 per cent; the erythrocytes numbered 3,610,000, and the leukocytes 9,500. Roentgenograms of the gallbladder by the Graham-Cole technic disclosed a faint shadow.

Because of the uncertainty of diagnosis the patient was kept under observation in the hospital for several weeks. Shortly after admission she began having mild attacks, and the possibility of neurocirculatory asthenia with paroxysmal tachycardia was considered. In a severe attack, July 4, it was noted that the blood pressure rose to 280 systolic and 180 diastolic. July 10 I made the suggestion that the condition might be considered one of intermittent paroxysmal hypertension of unknown origin, but probably on the basis of generalized vascular spasm.

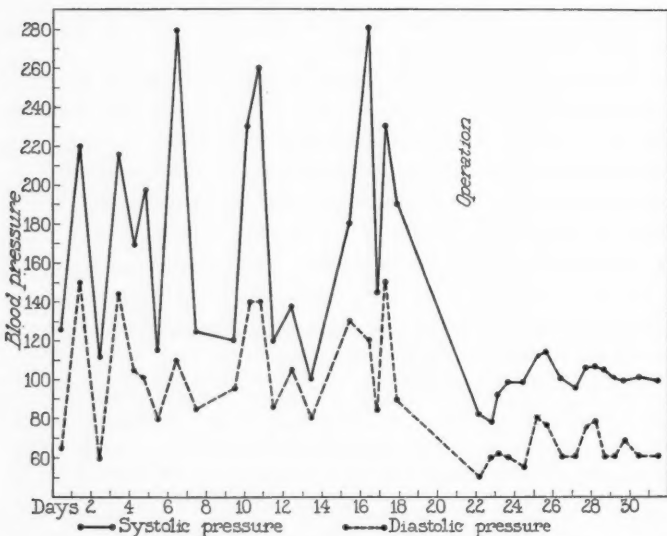


Fig. 265.—Changes in blood pressure on various days.

The attacks varied in severity and frequency. At times they occurred daily, again twice daily, and occasionally the patient would be free for one or two days. They came on most often after breakfast, so the patient thought they were due to some article of food. Moving about in bed or walking also seemed to bring on attacks. Prostration and slight abdominal distress, chiefly on the right side, followed. In detail, the attacks subjectively were characterized by "heart consciousness," palpitation, severe occipital headache, at times extending down to the upper dorsal region, nausea, vomiting, choking sensation, dyspnea, cough, dull tight sensation in the chest, at times becoming painful, coldness of the extremities, weakness, some trembling, at times numbness and tingling in the extremities, and occasionally blurring of

vision. With later attacks there was severe pain in the lower part of the abdomen and at times in the lumbar region. The patient became extremely prostrated and could not eat for several hours. She did not lose consciousness, however.

Objectively, the patient first showed an anxious facial expression during an attack. The pupils dilated slightly. There was pallor of the body with cold perspiration. Around the eyes, nose, and mouth appeared reddish-purple mottling. In the later attacks this extended to the upper part of the chest. The veins of the neck were unusually distended. The pulse rate was moderately accelerated. The blood pressure was markedly elevated, occasionally exceeding 300 systolic and 180 diastolic (Fig. 265). As an attack passed off the blood pressure dropped rather rapidly. There was frothy sputum, at times blood-tinged and accompanied by signs of pulmonary edema, which cleared rapidly with the decrease in blood pressure. The heart enlarged moderately during attacks.

Special studies of the changes demonstrated that the blood pressure increased prior to the elevation of the pulse rate. There was not any visible change in the fundi of the eyes. Brown studied the peripheral capillaries. The capillaries of the nail-fold became entirely obliterated when the systolic blood pressure reached 170 mm., and did not reappear until it had declined to this level. An electrocardiogram did not reveal changes except in the heart rate. A great many drugs were used in an attempt to prevent or abort the attacks, including digitalis, quinidin, amyl nitrate, bromids, chloral, phenobarbital, belladonna, potassium iodid, morphin, typhoid vaccine, histamin, and cholin. However, there was not any definite benefit from any of these.

Because of the belief that the attacks were in some way mediated through the sympathetic nervous system, and that an approach through the splanchnic nerves might prove beneficial, and because of the increasing abdominal pain, surgical consultation was requested with a view to abdominal exploration. The patient was seen by C. H. Mayo. Operation was performed October 9 through an upper median-line incision. The gallbladder was fairly normal, the appendix had been removed previously, and there were no adhesions. The stomach and duodenum were normal. "The left suprarenal body was twice the normal size and the right apparently slightly enlarged. There was an oval mass, about 6 by 4 cm., situated retroperitoneally behind the tail of the pancreas on the mesial side of the left kidney and impinging against its upper pole. The capsule of the tumor was opened retroperitoneally and the tumor enucleated intact. The bleeding was excessive from a plexus of veins around the tumor; normally the veins of this area are large and connect with the spleen, tail of the pancreas, fundus of the stomach, and venous plexuses. The process of separating the tumor and breaking the many strands of attachments extending through the periphery of the capsule would remind one of excision of the superior sympathetic ganglion. The tumor was removed in its capsule and proved to be nerve tissue, probably an enormous malignant ganglion."

Convalescence was uneventful for two weeks; then pulmonary infarction developed, the signs of which lasted about ten days. The paroxysms of

hypertension have not recurred, and the patient since operation has been entirely free from headache, tachycardia, dyspnea, and vomiting. The systolic blood pressure has never been more than 120. The patient's general health has also improved greatly, her weight having increased 30 pounds (13.6 kg.).

This case was extremely interesting because of (1) the obscurity of the diagnosis, (2) the nature of the operative findings, and (3) the immediate and permanent relief from operation. No other case of hypertension in my entire experience has given me so much food for thought.

This case is similar to those in the group of vascular crisis described so aptly by Pal in 1905. It represents, however, an instance of general vascular spasm. Pal distinguished various types of local spasm: (1) Abdominal, as in lead-poisoning, and gastric, as in tabes; (2) cardiac, as in angina pectoris; (3) cerebral, with temporary evanescent attacks of paresis or aphasia; (4) retinal, as in temporary amaurosis; and (5) peripheral, as in Raynaud's disease. Increased blood pressure, of course, has also been encountered in renal or biliary colic.

In this case, however, vascular spasm was of a general nature, resulting in sudden and marked increase in blood pressure and the development of the signs and symptoms of advanced or even malignant hypertension. The spasm probably resulted from marked generalized stimulation of the vasoconstrictors of the body and corresponded in general to the local forms of spasm. There is the additional possibility, however, that it may have been caused by the sudden excretion of epinephrin or an epinephrin-like substance. During the attack the patient appeared to be the subject of a malignant form of hypertension which was indistinguishable from the ordinary picture of the disease and differed only in that it was intermittent rather than continuous in character. These attacks were unquestionably due to functional changes in the vessels or vasomotor center, secondary to tumor of the retroperitoneal nerve. Removal of the tumor resulted in immediate and, to date, permanent cure.

Case 5. Paroxysmal hypertension with chronic appendicitis and chronic cholecystitis.—A woman aged thirty-five came to the Clinic in January, 1927, complaining of intermittent heart attacks during the previous three months. There was nothing of significance in the family history. The patient's history included an abdominal injury at seventeen with persistence of the tumor, diphtheria, and rheumatic fever in childhood, influenza and pneumonia nine years before, and herpes and purpura during the year preceding admission to the Clinic. Two cesarean sections had been performed, one twelve years and another fourteen months previously. The first of the heart attacks, which were her chief complaint, came at the end of a strenuous day. At first the heart beat so slowly that she thought it would stop, then its action was accelerated. She felt giddy. Precordial pain, radiating to neck and down the left arm to the elbow, was present. There was a sense of oppression in the chest, dark spots before the eyes, and a feeling of nausea. These attacks had been recurring with greater frequency and severity and she had been in the hospital during two attacks; morphin had given relief. She also complained of frequent nausea and chronic constipation, for which daily colonic irrigations and frequent laxatives were necessary. There had been tenderness in the right lower quadrant following an attack of abdominal distress with nausea eight months previously. She also complained of a nonproductive cough, slight rise in temperature daily, and daily headaches, sometimes with nausea.

The patient was obese, weighing 178 pounds. The systolic blood pressure was 135, the diastolic 75. The pupils reacted sluggishly to light. There was tenderness in the right lower quadrant of the abdomen. The chest was clear and the pelvis negative. Examination of the eyes was essentially negative, although the right disk was pale, full, and blurred nasally with definite colloid excrescences; the left disk was glassy as the result of an excess of glial tissue and the retinal arteries were of relatively small caliber.

During a typical attack the patient was weeping, with her hand over her heart, and complaining of precordial pain radiating to the root of the neck. The pulse was rapid and difficult to obtain. There were sharply defined deep scarlet areas on the face, neck, and upper part of the thorax which blanched on pressure. The systolic blood pressure rose to 180, the diastolic to 100, gradually decreasing to 140 systolic and 80 diastolic.

In an effort to induce an attack drugs such as ephedrin and epinephrin were used. Twenty-five milligrams of ephedrin by mouth produced no appreciable effect. Three minims of epinephrin produced the subjective features of the spontaneous attacks, but there was no significant rise in blood pressure.

The basal metabolic rate was $+2$; urinalysis was negative; renal function was normal; the hemoglobin was 65 per cent, erythrocytes numbered 3,320,000, and leukocytes varied from 6,600 to 9,700. Roentgenograms of the chest, kidneys, ureters, bladder, and gallbladder were negative. The electrocardiogram showed a rate of 85 and sinus rhythm. A gastric test-meal showed no free hydrochloric acid. The blood sugar was 0.95 per cent for each 100 c.c., but was as high as 1.09 per cent during an attack.

Because of the gastro-intestinal complaints and history operation was

performed, and the gallbladder and appendix, both infected, were removed. Convalescence was uneventful. Two months later there had been no recurrence of the attacks.

In this case the evidence of functional disturbances in the central nervous system was marked. The patient was of a psychic type and emotional. However, the gallbladder and appendix, both of which were infected, might have been playing a rôle. It was questionable also whether this case should be regarded as true intermittent hypertension. The only certain factor was that the patient's blood pressure was high during attacks. Paroxysmal tachycardia is most frequently associated with a drop in blood pressure, but the tachycardia which is present in gall-bladder attacks is sometimes associated with increase in blood pressure. As the cause of increased blood pressure overactivity of the heart as well as constricted vessels must be kept in mind.

Case 6. Paroxysmal hypertension.—A man aged thirty-nine came to the Clinic in November, 1927. His father had died from apoplexy at the age of sixty-three. The history included scarlet fever, mumps, pertussis, and diphtheria in childhood, with frequent attacks of tonsillitis until removal of the tonsils in 1917. He had had influenza in 1919. The chief complaint was that he was subject to "spells" of dyspnea, and epigastric distress, radiating up the chest and neck to the back of the head. He had been having these attacks for a year and a half and they had been increasing in severity and frequency. They usually lasted from ten to fifteen minutes, but the length of time had varied from five minutes to two or three hours. He had had at least one spell every day and occasionally four or five daily. They were accompanied by palpitation and a desire to urinate, although the act itself was impossible. The hands and arms became numb and the entire body assumed a sickly yellowish color. The attacks were sometimes accompanied by marked perspiration, and occasionally by severe nausea and vomiting. Twice during the spells he fell, although he did not lose consciousness. Twice carpal spasm occurred in connection with the attacks.

The skin was dark, although of normal texture. The head, neck, and chest were normal and the fundus examination was negative. The edge of the liver was palpable about 3 cm. below the costal margin. There was no infection of the prostate or vesicles. Urinalysis was negative except for an occasional trace of albumin. The phenolsulphonephthalein return was 45 per cent. The leukocytes numbered 14,800 and the differential count was normal. The blood urea varied from 16 to 46 mg. for each 100 c.c., the calcium was 10.9 mg., and the blood sugar 0.116 per cent. The Wassermann

test was negative. Tests of hepatic function showed no dye retention and the serum bilirubin was normal. The electrocardiogram gave a rate of 68, the complex QRS in Leads I and III was slurred, and notched in Lead II, and there was left ventricular preponderance and inverted T-wave in Lead I. Roentgenograms of the chest and gallbladder were negative. No changes in the mediastinum or stomach could be detected.

In an attack first the hands appeared somewhat mottled, then there was pallor of the entire body. The systolic blood pressure went as high as 228, the diastolic 120, but responded to the administration of amyl nitrite, being reduced to 108 and 52, although the patient insisted that there was no change in the subjective symptoms.

Attempts to induce attacks by the administration of ephedrin and epinephrin failed completely, but the patient could induce them at will by leaning over the foot of the bed or over the back of a chair in such a way as to exert pressure on the abdomen. His wife, however, objected to any further demonstration of this kind. The possibility of diaphragmatic hernia or some other intra-abdominal abnormality was seriously considered because of the postural relationship of the attack. However, proof was lacking. Exploration was not urged, but the patient planned to return if the attacks persisted.

The next case represents an entirely different type of disease and brings up the question of relation of blood pressure to blood volume.

Case 7. Polycythemia vera, hypertension, possibly Geisbock's disease or polycythemia hypertonica.—A farmer aged fifty-seven came to the Clinic in April, 1925, complaining of headaches, nausea, vomiting, vertigo, ringing in ears, blurring of vision, loss of appetite, and constipation. Illness had included rheumatic fever in 1887, influenza in 1920, and an operation in 1918 for the removal of a neuroma in the left popliteal space. Until the autumn of 1922 he had been able to carry on the work on the farm as usual. At that time he was troubled with pain in the right shoulder and right arm which was diagnosed neuritis. It cleared up in two weeks, but then headaches in the occipital region, frequently radiating to the frontal region, appeared. These headaches occurred every three or four days, usually in the evening, and lasted for three or four hours. They were usually accompanied by nausea and vomiting. During the last year he had also been troubled with dizziness, and blurring of vision came on suddenly about two months before admission to the Clinic.

The patient appeared well developed and well nourished. The extremities and the lips and tongue were cyanotic and the fauces deeply injected. The lower part of the right leg was swollen and tender, but no local vascular changes could be observed in the roentgenogram. The aortic sounds were accentuated. The chest was normal. The spleen was just palpable. The systolic blood pressure was 192, the diastolic 140. Urinalysis showed albumin, pus, and red blood cells; the specific gravity varied between 1.023 and 1.012. The erythrocytes numbered 8,530,000, the leukocytes 6,700; the hemoglobin

was 29.4 gm. and the blood viscosity was 12. There was no dye retention in the test of hepatic function and the serum bilirubin was 0.9 mg.

Treatment with phenylhydrazin was instituted, 1.5 grains being given twice daily for seventeen days, a total of slightly more than 6 gm. Five days after treatment was stopped thrombosis developed in the left basilic vein. Under treatment the erythrocytes were reduced to 2,180,000, the hemoglobin to 12.5 gm., the viscosity dropped to 4.1, and the leukocytes were increased to 15,000. The serum bilirubin went as high as 2.4 and 4.3 mg. (Fig. 266).

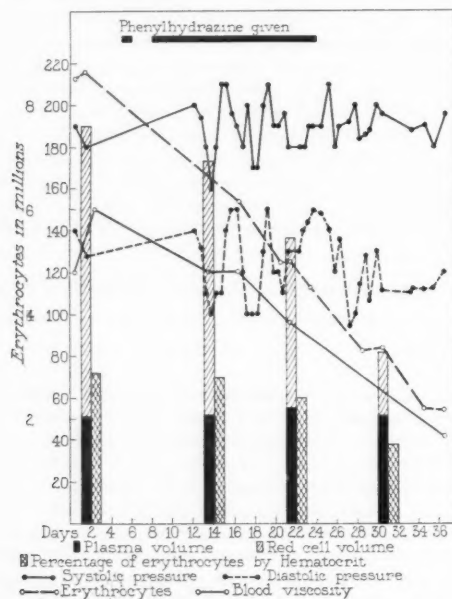


Fig. 266.—Effect of phenylhydrazin on the blood and plasma volume, erythrocytes, and hemoglobin, and the absence of its effect on the blood pressure.

When the patient was dismissed he was free from headaches and dizziness. He was advised to use phenylhydrazin as needed. The accompanying chart prepared by Dr. Peacock presents all the important data (Fig. 266).

This case is of interest because (1) it combines the features of polycythemia vera and essential hypertension, (2) it raises the question of whether or not such an entity as Geisbock's disease or polycythemia hypertonica exists, and (3) it demon-

strates that hypertension may be altogether independent of the blood volume, since hypertension was undiminished although the blood volume was reduced to 40 per cent of its former amount.

It is of unusual significance that hypertension is usually absent in polycythemia vera despite the existence of tremendous increase in the blood volume and accompanying increase in the viscosity of the blood. An analysis of such cases by Dr. Peacock indicates that hypertension was present in only eight of fifty cases. This would seem to be too high an incidence to be purely accidental. On the other hand, in this case there was evidence that the reduction of the blood volume and of the blood viscosity by phenylhydrazin has in no way affected the hypertension.

The relation of blood volume to blood pressure calls for further investigation. Its influence is probably much less than would be anticipated. Studies of blood volume with the dye method have revealed the fact that in hypertension the blood volume is, as a rule, not only not increased but actually less than normal. As has been shown, the blood pressure is normal in the majority of cases of polycythemia vera. On the other hand, it should be recognized that marked decrease in blood volume from normal levels may materially affect the level of the blood pressure, at least the blood pressure is usually low following marked hemorrhage and also in surgical shock.

It is interesting now to revert to the factors which determine blood pressure as postulated by Janeway. Concerning the energy of the heart information is inadequate; however, time has not contributed much to the idea that hypertension is due primarily to overactivity of the heart. The rôle of the heart would seem to be secondary in the effort to meet peripheral resistance. The peripheral resistance (probably of both capillaries and arterioles) obviously is the important consideration. The elasticity of the arterial wall is unquestionably of importance, while the blood volume is relatively insignificant. To my mind one great factor has never received adequate consideration, that is, vasoconstriction brought on by the sympathetic system.

The changes in the color of the skin accompanying the use of amyl nitrite and also the marked and sudden drop in blood

pressure of patients with hypertension or vascular constriction impress me with the functional aspects of hypertension and also with the importance of the rôle of the vasoconstrictors. The cure of Raynaud's disease of the feet by lumbar ganglionectomy still further emphasizes the importance of the nervous mechanism in controlling the peripheral vascular bed. The complete disappearance of the symptoms of hypertension which followed lumbar sympathectomy in Case 3 leads me to believe that relief from malignant hypertension should be sought in surgery. The study of Case 4 indicates to me that functional spasm of all the vasoconstrictors of the body can reproduce the clinical picture of hypertension, that such spasms may be initiated in the sympathetic nervous system, and that it is possible for correction of an anomaly of the central nervous system to effect cure.

Recognition of the fact that vasoconstriction, if general, may result in hypertension, if local, in such diseases as Raynaud's disease, lead colic, amaurosis, angina and transient hemiplegia, raises many pertinent questions. Is local vasoconstriction playing an unrecognized rôle in other diseases such as duodenal ulcer, diabetes mellitus, and nephritis? Can release from vascular spasm be sought through surgery? It seems to me that the surgeon should develop a working interest in this field, more particularly since in one type of vascular disease (Raynaud's disease and other vascular diseases of the feet) surgical treatment has been so eminently successful.

CLINICALLY ARRESTED THROMBO-ANGIITIS OBLITERANS

EDGAR V. ALLEN

THROMBO-ANGIITIS obliterans is not rare, as is shown by published percentages. In 1926, one of each 600 male patients registered at the Mayo Clinic was afflicted with this disease in some form. The ratio for the year 1927 has not as yet been determined, but it is greater. Libman has stated that Buerger is of the opinion that the disease is spreading and is now mildly endemic.

Prognosis in the past has been pessimistic, as witness the slogan "high and early amputation" based largely on an opinion that radical amputation will be necessary eventually. Meyerding and I have shown that conservative surgical measures are often successful, that toes may be amputated without fear in carefully selected cases, and that amputation below the knee except in cases complicated by unusually extensive gangrene, edema or cellulitis is followed by healing in approximately 80 per cent of cases. There remains a group in which minor operations or none at all are necessary. New physiologic concepts of the disease, new and more extensive methods of medical treatment, and careful investigation of late results have shown the necessity of abandoning the pessimistic attitude in many cases; clinical evidence of arrest is seen, and the disease may run its entire course, excluding extensive gangrene, without prejudice to recovery of function adequate for the ordinary physiologic demands. This is a relatively recent concept and serves as the basis for the presentation of the following cases. Future observation of other cases over longer periods of time will doubtless disclose many with more marked evidence of arterial compensation.

REPORT OF CASES

Case 1. Thrombo-angiitis obliterans arrested for five years in the left foot, active in the right foot; history of superficial phlebitis.—A Scotch-Irish factory foreman aged forty-eight entered the Mayo Clinic October 14, 1925 complaining of pain, numbness, and swelling of the right great toe. He had smoked forty cigarettes a day for many years. Five years previously pain had developed in the left arch after exercise, followed shortly by migratory superficial phlebitis over the left leg and foot. Six months later a small ulcer occurred on the second left toe, followed by swelling, redness, and lymphangitis extending to the groin. The toe became gangrenous and was amputated. Healing was satisfactory. During the next five years the only symptom in either foot was mild pain in the left arch after excessive exercise. Ten months before admission there had been pain in the arch of the right foot after exercise, and five months later migratory phlebitis had appeared over the right leg and foot. Two months before admission the patient observed rubor of the right toes when they were in the dependent position. Five weeks before admission a spontaneous ulcer appeared on the dorsum of the right great toe. General examination was essentially negative except for the lower extremities. Both feet were cold, the right more so. The circulatory efficiency test* showed rubor, graded 2, with the foot in the dependent position (0°) and pallor, graded 4, at 180°. There was a shallow gangrenous ulcer around the base of the right great toe nail. The second and third toes of the left foot had been amputated. The arteries of both upper extremities and both femoral and both popliteal arteries pulsated normally. The left dorsalis pedis and right posterior tibial arteries pulsated normally. Pulsations in the right dorsalis pedis and left posterior tibial arteries could not be felt. A diagnosis was made of thrombo-angiitis obliterans, well compensated in the left foot and active in the right.

A diagnosis of Buerger's disease was quite tenable in the presence of arterial obliteration, superficial phlebitis, positive tests of circulatory efficiency, symptoms of vascular insufficiency, and nonhealing trophic ulcers. This case is particularly interesting because the left foot had gone through a definite process of arterial obliteration with gangrene. This was followed by healing and almost complete disappearance of all symptoms for five years, which seems long enough to indicate permanent arrest. The arteries to this foot still showed evidence of obliteration, and the circulatory efficiency test was still positive. The circulation to the left foot had probably been reestablished by

* 180° indicates elevation of the foot from the standing position so that the leg forms a right angle with bed, 0° indicates the position with the foot dependent.

the utilization of available collateral channels and the canalization of the thrombus in the large arteries. The latter process can be demonstrated microscopically.

Case 2. Thrombo-angiitis obliterans arrested for three years in the left foot; distal thrombosis in the toes of the right foot.—A locomotive engineer aged thirty-three entered the Mayo Clinic December 8, 1923 complaining of a painful right fourth toe. Two years before he had noticed a burning sensation in the sole of the left foot, usually brought on by exercise. Soon afterward the third left toe became purplish and very painful; the toe was amputated. A similar condition necessitated the amputation of the fifth toe and, later, of the second and fourth toes. Healing did not occur for one year. One year before admission pain began in the toes of the right foot with purplish discoloration and mild trophic ulcers which healed slowly. In the last two years the patient had noticed that the feet had become progressively colder and that all symptoms were worse in cold weather. General examination was essentially negative except for the extremities. The feet were cold, and all the toes on the left foot except the great toe were absent. The wounds were well healed. The right foot appeared normal. Tests of circulatory efficiency in both feet showed blanching, graded 1, when elevated, and rubor, graded 2, when dependent; the right and left popliteal and femoral arteries pulsated normally. Both dorsalis pedis arteries were pulseless, and pulsations in both posterior tibial arteries were diminished. The diagnosis was thrombo-angiitis obliterans, and the patient was dismissed, following convalescence after uneventful tonsillectomy, with instructions for the care of the feet. He returned in March, 1926 complaining of discoloration of the second and third toes of the right foot. In the two years following the first admission there had been no symptoms in the left foot although it had remained cold. General examination at this time was essentially negative except for the extremities. The hands and feet were cold. There were no pulsations in both ulnars and left dorsalis pedis; pulsations were markedly diminished in both posterior tibials and right dorsalis pedis, and slightly diminished in both radials and both popliteals. Test of circulatory efficiency at 180° showed in the right foot pallor, graded 3, and in the left pallor, graded 1; at 0°, rubor of both the right and left, graded 3. The diagnosis was thrombo-angiitis obliterans, compensated in the left foot and with distal thrombosis of the vessels of the second and third toes of the right foot. The second and third right toes were amputated and healing was satisfactory. Microscopic examination of the amputated toes showed vascular obliteration, the lesion being considered typical of thrombo-angiitis obliterans.

A diagnosis of thrombo-angiitis obliterans was made tenable by the age of the patient, the evidence of arterial obliteration, the positive circulatory-efficiency tests, the occurrence of spontaneous, slowly healing trophic ulcers, and the absence of demonstrable arteriosclerosis and diabetes. The point of chief interest

in this case was the apparent complete compensation of circulation in the left lower extremity as evidenced by absence of symptoms for three years. Circulation was adequate, although there was evidence of more obliteration in the large arteries in the left leg than at the previous admission. The improvement in the circulation during the course of the disease was probably the result of the utilization of collateral circulation and the canalization of the thrombi in the larger arteries.

Case 3. Thrombo-angiitis obliterans compensated for eighteen months in the right foot; healing of ulcers of the toes of the left foot.—A Hebrew aged thirty-two entered the Mayo Clinic December 28, 1926. Ten years before he had suffered from pain in the calves of both legs on exercise. This was rather intermittent in character and slowly progressive, but had disappeared in both calves five years previously. Five years before admission a small ulcer appeared spontaneously on the tip of the right great toe, and was associated with moderate pain. Healing occurred after six months. Three and a half years before admission a small ulcer appeared on the left great toe and healed in six months. Two years before admission a small ulcer occurred on the under surface of the right great toe and healed in four months. One and a half years before admission a small lesion occurred on the under surface of the right great toe, and one on the right fifth toe. The former healed in four months, the latter in three. Six months before admission there was severe pain in the left foot on exercise. It prevented ordinary exercise, and compelled the patient to stop work. Four months before admission an ulcer appeared on the tip of the left great toe which gradually spread until the entire toe had become gangrenous.

General examination was essentially negative except for the extremities. There was gangrene of the left first and second toes. The left foot was cold and the right almost normally warm. Tests of circulatory efficiency were satisfactory on the right side, but at 0° there was rubor, graded 2, on the left. Pulsations were normal in the left radial, both ulnar and both femoral arteries, diminished in the right radial, the right popliteal and right dorsalis pedis arteries, and absent in both posterior tibial and left dorsalis pedis arteries.

The diagnosis was thrombo-angiitis obliterans, compensated in the right and active in the left. After intensive therapeutic measures, gangrenous areas became demarcated, and there was indication of healing of the first and second toes of the left foot. Six months later the physician of the patient wrote that the lesions were completely healed.

A diagnosis of thrombo-angiitis obliterans was tenable in view of the age and race of the patient, the evidence of arterial obliteration, and the recurrence of slowly healing trophic ulcers. There had been no symptoms in the right foot for one and a half

years. At the time of admission there was no evidence of vascular disease in the right foot other than the obliterated posterior tibial artery, but the previous occurrence of gangrene of the toes of the right foot and the pain of claudication in the right calf indicated insufficient blood supply. The disappearance of these symptoms, the normal warmth of the foot, the absence of trophic changes, and the absence of abnormal changes in color with change of posture indicated reestablishment of circulation in the right foot. The healing of the toes of the left foot indicated a similar process.

Case 4. Thrombo-angiitis obliterans clinically arrested for two years; successful amputation of toes; return of claudication in the calf after absence for five years.—A man aged forty-nine came to the Mayo Clinic January 2, 1925 complaining of sore feet and discoloration of the tip of the second toe on the right foot. Ten years before, exercise had caused claudication in the calves. This lasted for one month, and disappeared for five years. In the summer before admission persistent aching began in the calves, and in the winter became so severe that it interfered with sleep and ordinary daily routine. The pain increased in severity. Four months before admission most of the pain had localized in the right leg and foot, and was sharp, stinging, and throbbing. For six weeks the patient had been unable to sleep without hanging the right leg out of bed. For the last two years there had been numbness, swelling, aching, claudication, and pain in both hands when at rest. During the same period there were recurrent attacks of superficial phlebitis in the legs, thighs, and arms. Three weeks before admission a cow had stepped on the right foot and injured the second toe slightly. Severe pain followed, and a blood-blister appeared which was opened by the patient. The tip of the toe became gangrenous, and an ulcer appeared and persisted. In the last year the patient had lost 20 pounds in weight.

General examination was essentially negative except for the extremities. Both feet were cold, cyanotic, and perspiring. The skin and nails of the toes of the left foot were thickened and roughened. The second toe of the right foot was gangrenous, and there was edema of the ankle, graded 3. The skin was tense, shiny, and reddened. The left ulnar and radial arteries, the right ulnar, and the arteries of the right foot and leg were pulsating normally. The dorsalis pedis and posterior tibial arteries of the left foot were pulseless. The right radial artery showed diminished pulsation. The left foot showed pallor, graded 3, when elevated; and rubor, graded 2, when dependent. The right foot showed pallor, graded 3, when elevated; and rubor, graded 2, with bluish cyanosis when dependent.

The usual laboratory tests were negative. A diagnosis was made of thrombo-angiitis obliterans of both feet, compensated in the left and active in the right, with gangrene of the second toe.

Gangrene progressed, and pain became more severe in the second toe of

the right foot and it was amputated at the proximal joint. Healing was satisfactory. Seventy-two days after admission the patient was dismissed from observation free from pain and with a well-healed amputation stump. Two years later he was free from symptoms except for slight aching in the feet in cold weather.

Microscopically, one of the main arteries of the toe was patent and did not show thrombosis. The other arteries and the veins were occluded by partially organized thrombi. There was marked vascularization of the periarterial fibrous tissue, but there was no evidence of acute infection.

The diagnosis of thrombo-angiitis obliterans was based on the presence of arterial obliteration, superficial phlebitis, changes in color with change of position, the pain of claudication, and the trophic changes. Microscopic study confirmed the diagnosis. The symptoms definitely indicated vascular insufficiency. Healing of the amputation wounds was due to an adequate blood supply through normally pulsating arteries. Two years of complete absence of clinical evidence of arterial insufficiency indicates a condition of quiescence and justifies the assumption that arterial compensation was present in the left lower extremity.

DISCUSSION

The pathologic changes of thrombo-angiitis obliterans produce their effects largely by one process: diminished volume flow of blood for each minute through the extremities. The term minute volume is used to indicate this. Prognosis, therefore, depends on the degree and rapidity of interference with the minute volume of the blood. The changes in the arteries of the extremities may be visualized as (1) obliteration of the larger arteries causing diminution of the minute volume of blood, and (2) an attempt by physiologic means to keep the total minute volume at a level high enough to meet the physiologic demands. The latter is accomplished in two ways: canalization of the old thrombi in the larger arteries, and increased minute volume through arteries not affected by the obliterative process. These two processes of obstruction and compensation are mutually antagonistic, and the clinical course depends on which predominates. Early in the course of the disease there is uniformly a gradual diminution in the total minute volume through the extremities. This may

progress inevitably to gangrene, necessitating amputation, or, much less frequently, reach a condition of equilibrium which may be followed by an increase in the minute volume of blood through the extremities. The usual obliterative process is slow and allows the development of collateral circulation. Moreover, it is inflammatory in nature and in any area must eventually become quiescent. Thus, although thrombo-angiitis obliterans is a self-limiting disease, the problem is to prevent gangrene before limitation is reached. Two processes dispose to an unfavorable prognosis by virtue of their effects on the minute volume of blood flowing through any part of the extremity; one is rapidly progressive occlusion of the larger arteries, and the other is extension of the obliterative process into the collateral vessels. The former is so rapid that available collateral vessels cannot compensate sufficiently, and the latter prevents compensation by obliterating them. A favorable prognosis is determined by a slowly obliterative process which becomes stationary and leaves a large enough portion of the arterial tree to keep the minute volume adequate for the ordinary physiologic demands. I do not believe it is justifiable to call these lesions healed. Further observation is needed, and at present these cases can be designated only as clinically arrested cases with adequate arterial supply.

I am of the opinion that the degree and rapidity of interference with the total minute volume through any part of the extremity can be determined clinically with sufficient accuracy for practical purposes by the severity of the pain during rest. I have noted frequently that when pain during rest is severe and intractable, amputation is invariably required; and when pain is mild or absent, trophic changes are either absent or so slight that the lesions often heal. This affords a clue, inaccurate to be sure, by which the type of case in which eventual compensation can be expected may be roughly determined in advance. When the history is long and the pain at rest mild the outlook is bright; when the history is short and the pain severe it is gloomy. A survey of the cases presented here shows that the history was long and the pain at rest mild or absent, indicating

a slowly progressive obliterative process with the coincidental establishment of greater arterial circulation in unaffected channels and the maintenance of the total minute volume of blood at an adequate level. The marked clinical improvement in these cases doubtless indicates the achievement of the aim of all medical and some surgical (for example, lumbar ganglionectomy) forms of treatment: the increase in the total minute volume flow of blood.

SUMMARY AND CONCLUSIONS

A pessimistic prognosis is not always warranted in cases of thrombo-angiitis obliterans, as compensation of the total minute volume flow of blood may occur and the extremities be supplied with sufficient blood for ordinary physiologic demands. Four cases are presented to illustrate this contention.

HYPERTENSION AND POLYCYTHEMIA: THE SO-CALLED GEISBOCK'S SYNDROME

BAYARD T. HORTON

THE term polycythemia is used to designate conditions in which the number of erythrocytes in each unit volume of blood is above normal, the normal in man being usually taken as 5,000,000 for each cubic millimeter. Polycythemia may be divided into two groups: (1) absolute polycythemia, in which the total number of circulating erythrocytes, as well as the number for each unit volume of blood, is increased, as in polycythemia vera, and (2) relative polycythemia, in which there is no actual increase in the number of erythrocytes in the body, but a greater concentration in the blood as obtained in dehydration states when plasma is abstracted from the blood.

The cases presented here are examples of those in which a consideration of polycythemia was indicated because of the high percentage values for the erythrocyte and hemoglobin determinations. The important point in the diagnosis was the determination of the presence or absence of polycythemia vera. The most important single diagnostic observation in polycythemia vera is the existence of marked increase in the total and relative blood volume as determined by the dye method. In many hundred examinations by the dye method in normal and pathologic subjects, values of more than 115-120 c.c. for each kilogram of body weight are extremely rare. The presence of an enlarged spleen, erythema, reddish cyanotic color of the extremities and the exposed areas of skin and mucous membrane, and engorged cyanotic appearing veins of the retina are additional confirmation of polycythemia vera. If an untreated case of polycythemia vera is eliminated by a study of clinical symptoms and blood volume, there still remains a group of subjects who

have an increased number of erythrocytes for each cubic millimeter of blood, high values for percentage of hemoglobin, and fairly normal values for the blood volume, on the basis of body weight. The final classification of these cases is sometimes most difficult. Pathologic conditions in which anoxemia is present and in which there is a compensatory increase in the number of erythrocytes in the circulating blood can be ruled out. Frequently the chief clinical data are related to the abnormal redness of the face, occasionally the mucous membranes, and the high relative blood values.

POLYCYTHEMIA VERA OR VAQUEZ'S DISEASE

Case 1.—A man aged fifty registered at the Mayo Clinic June 6, 1927 complaining of weakness and of being generally fatigued. The history was negative except that two ribs had been fractured in 1926 and he had had pneumonia at that time. Two years before admission a tooth had been extracted and bleeding had followed for four days. The estimated loss of blood was 2,000 c.c. Six months later a second tooth was extracted and was followed by prolonged bleeding. Since that time the patient had been suffering from progressive weakness, and had had to force himself to do even light work.

Erythema, graded 1, of the entire surface of the skin, except the face, hands, and feet, was noted. Cyanosis of the latter surfaces and of the buccal mucous membrane was graded 3. The conjunctiva was markedly congested. The spleen and liver were enlarged. The liver extended 6 cm. and the spleen 10 cm. below the costal margin in the median clavicular lines. The systolic blood pressure was 126 and the diastolic 102. The urine was normal and the Wassermann test of the blood and roentgenograms of the chest were negative. Infection of two teeth was revealed by the roentgen ray. The hemoglobin was 156 per cent by the acid hematin method. The erythrocytes numbered 6,810,000 and the leukocytes 9,600; differential count revealed lymphocytes 7.5 per cent, large mononuclears 1.5 per cent, transitionals 2.5 per cent, neutrophils 83.5 per cent, eosinophils 3.5 per cent, and basophils 1.5 per cent. The bleeding time was two minutes, coagulation time ten minutes, and calcium coagulation time thirteen minutes. The prothrombin time was normal. The viscosity of the blood was 15 (normal viscosity 4.5). The basal metabolic rate was +22. The total blood volume was 16,000 c.c., or 246 c.c. for each kilogram of body weight (normal 70 to 100 c.c. for each kilogram of body weight), whereas the cell volume by hematocrit was 72 per cent (normal from 40 to 44 per cent).

After treatment by phenylhydrazin and venesection, the total blood volume was 7,810 c.c., or 118 c.c. for each kilogram of body weight, whereas the cell volume by hematocrit was 53 per cent. Viscosity of blood was 7.5. The erythrocytes numbered 4,940,000 and the leukocytes 25,000; the differ-

ential count revealed lymphocytes 10.5 per cent, large mononuclears 7 per cent, transitionals 4 per cent, neutrophils 80.5 per cent, eosinophils 3 per cent, and basophils 1 per cent.

Following treatment there was definite improvement. The patient was mentally clear, he felt ambitious, and was ready to go back to work. There was decrease in the size of the liver and spleen after the treatment; the edge of the liver was 4 cm. and the spleen 6 cm. below the costal margin in the median clavicular line. Diffuse erythema was still present on the patient's dismissal from the hospital, although less marked than on admission. The clinical diagnosis was polycythemia vera, arteriosclerosis, and dental sepsis.

This patient represents an example of true or absolute polycythemia. The enlarged spleen, palpable liver, color of the skin, and huge increase in the absolute and relative volumes of blood, and percentage of cells by the hematocrit, determine the diagnosis. Excessive bleeding following extraction of teeth is frequently observed in cases of polycythemia vera. The usual symptoms and signs in this disease are weakness, and those indicating cerebral irritability, such as dizziness, headaches, and emotional changes. There is usually a history of vascular accident, such as thrombosis. The treatment consists in the reduction of the huge number of erythrocytes. Phenylhydrazin hydrochlorid accomplishes this purpose, but must be used with caution. The untoward sequelæ of this treatment are the additional tendency to thrombosis and excessive destruction of blood. This treatment should be used with a great deal of caution in persons more than sixty years of age. The symptoms usually are alleviated with reduction in the number of erythrocytes.

POLYCYTHEMIA HYPERTONICA OR GEISBOCK'S SYNDROME

Case 2.—A woman aged forty-eight registered at the Clinic August 18, 1927 because of exhaustion, diminished vision, and loss of weight of two years' duration. She had had four children, the youngest aged seventeen and the oldest aged twenty-seven years. She had had diphtheria in childhood, and influenza two years prior to admission. During the last three years she had noticed a feeling of fullness in the head, and for the last six months failing vision. The blood pressure had been high for two years. She had lost 40 pounds in weight during the last four months.

The patient appeared well nourished and well developed, talkative, and mentally alert. The systolic blood pressure was 220, the diastolic 150. The eyes were prominent; the pupils reacted normally, and the media were clear.

There was bilateral edema of the disks (4D) with cotton-wool exudates around the disks and along some of the veins. The retinal arteries were visible and appeared constricted. The veins were slightly engorged. The ocular movements were normal, and the fields seemed normal. Cardiac dullness extended 12.5 cm. to the left of the median sternal line. There was ringing accentuation of the aortic and pulmonic second sounds, with a soft systolic murmur over the entire precordia. The rate and rhythm were regular. The edge of the liver extended from 2 to 3 cm. below the costal margin. The spleen was not palpable. There was sclerosis, graded 2+, of the peripheral arteries. The neurologic examination revealed arteriosclerosis of the central nervous system.

The urine contained albumin, graded 3, with hyaline casts, and 6 pus cells to the high-power field. The blood Wassermann test was negative; blood urea was 26, creatinin 1.5, and the phenolsulphonethalein return was from 45 to 55 per cent. The electrocardiogram did not show definite changes. The erythrocytes numbered 7,370,000 and the leukocytes 15,800; the differential count showed lymphocytes 27 per cent, large mononuclears 5 per cent, transitionals 3 per cent, neutrophils 62 per cent, eosinophils 2 per cent, and basophils 1 per cent. The hemoglobin was 100 per cent (Dare); there were 20 gm. hemoglobin for each 100 c.c. of blood (normal 13.5 to 15 gm. for each 100 c.c.). The viscosity of the blood was 8.

The total blood volume was 7,500 c.c., or 110 c.c. for each kilogram of body weight, and the cell volume by hematocrit was 59 per cent. It was believed that repeated venesection and withdrawal of spinal fluid at intervals would be beneficial to the patient. Two thousand cubic centimeters of blood was withdrawn as a result of venesection on four occasions, and from 25 to 30 c.c. of spinal fluid was withdrawn on two occasions. Under this treatment, associated with rest in bed and the usual hypertension regimen, the patient improved definitely. The blood pressure was lower than on admission. The blood was practically normal cytologically. The diagnosis was essential hypertension of the malignant type and polycythemia of indeterminate type.

This case represents an example of essential hypertension of the malignant type, a form in which excessive high blood pressure, especially the diastolic, is usually exhibited. Ophthalmoscopic examination revealed edema of the disks, contracted arteries, and exudates and hemorrhages. The prognosis in this type of hypertension is usually grave. The condition of the blood was particularly interesting. The number of erythrocytes, percentage value of hemoglobin, the increased viscosity of the blood, and percentage of erythrocytes by hematocrit indicated a large increase in the cellular elements of the blood. The blood volume for each kilogram of body-weight was somewhat increased. The normal mean value is 89 c.c. for each kilogram

of body weight. This patient weighed 150 pounds (68 kg.); she had lost 40 pounds. She was 63.5 inches in height. In the presence of obesity the blood volume for each kilogram of body weight is less than normal, since the adipose tissue is not well supplied with blood. If the patient had been of normal weight for her height, about 120 pounds or 55 kg., she would have had 180 c.c. for each kilogram of body weight, a value probably pathognomonic of polycythemia vera. In the absence of enlargement of the spleen, the diagnosis of polycythemia vera was not tenable, and the syndrome suggested by Geisbock was considered. An analysis of the blood in several hundred cases of hypertension has shown a normal number of erythrocytes and percentage of hemoglobin. Occasionally counts of more than 5,000,000 are found. It is difficult to believe that the polycythemia described by Geisbock represents a clinical entity. Parkes-Weber is of the opinion that this form of polycythemia occasionally represents a response of the blood during the course of essential hypertension. We finally concluded that if this patient were observed for a time and no treatment given, splenic enlargement would probably be in evidence and polycythemia vera in an early stage and essential hypertension would be the ultimate diagnosis.

Case 3.—A man aged twenty-four first presented himself at the Clinic August 1, 1927, complaining chiefly of high blood pressure which had been present for more than a year. The history was essentially negative except for double herniotomy in 1926, and occasional transient attacks of left-sided pain confined to the splenic area. The hypertension had been discovered when he was examined for nervousness and restlessness. The only symptoms had been occasional slight blurring of vision.

The patient weighed 162 pounds; his height was 68 inches. There was erythema, graded 2, of the face, hands, and conjunctiva. The thyroid gland was palpable. The heart and lungs were normal except for mild tachycardia. An indefinite mass was outlined in the left upper quadrant of the abdomen. The spleen was not palpable. The systolic pressure was 178 and the diastolic 138. Temperature was 96.8° F. Ophthalmoscopic examination was essentially negative. The urine contained a trace of albumin and pus cells. The hemoglobin by the acid hematin method was 125 per cent; the erythrocytes numbered 6,190,000 and the leukocytes 6,400; the differential count showed lymphocytes 27 per cent, large mononuclears 1.5 per cent, transitionals 7 per cent, neutrophils 68 per cent, and eosinophils 2 per cent.

The viscosity of the blood was 7.1. The basal metabolic rate was +17. The Wassermann test on the blood and roentgenograms of the chest were negative. The total blood volume was 5,840 c.c. (82 c.c. for each kilogram of body weight) and the cell volume by hematocrit was 52 per cent. Urologic examination revealed the left kidney to be occluded and functionless.

August 8 left nephrectomy was performed, following which the patient recovered uneventfully. The pathologist reported extensive hydronephrosis with complete destruction of the kidney.

August 25 the cell volume by the hematocrit had dropped to 42 per cent. The blood pressure was 182 and 100. There was much improvement in the patient's color and in subjective symptoms. The final diagnosis was essential hypertension, relative polycythemia, and left hydronephrosis.

The increase in the number of erythrocytes and percentage of hemoglobin in this case raised the question of the existence of polycythemia vera. The spleen was not palpable. The blood volume showed normal values for body weight. The percentage of erythrocytes by the hematocrit was definitely high, and the viscosity was elevated. This case corresponds to the Geisbock syndrome or polycythemia hypertonica. There is probably no relationship between the renal mass and the polycythemia. It was observed that following the operation with the associated loss of blood, the hemoglobin, erythrocytes, and the percentage of cell volume by hematocrit had returned to normal. The red color of the skin had disappeared. The possibility that an early phase of polycythemia vera was being dealt with could not be absolutely eliminated.

Case 4.—A man aged fifty-five registered at the Clinic September 21, 1923 complaining of high blood pressure. The hypertension was discovered three months prior to the patient's admission to the Clinic while he was undergoing examination for life insurance. Occasionally he had had occipital headache early in the morning, but he had had no other symptoms.

The patient was obese, but he appeared to be in good health. He weighed 197 pounds, and was 68 inches in height. The systolic blood pressure was 180 and the diastolic 120. Both fundi revealed mild arteriosclerosis of the retinal arteries. All of the teeth were infected. The left border of the heart, on percussion, extended 11 cm. from the median sternal line. The rate and rhythm were regular. No murmurs were heard. Electrocardiogram was negative. A small umbilical hernia was present. The edge of the liver was palpable. The spleen was questionably palpable. Enlargement of the prostate was graded 2, and the bladder contained 30 c.c. of residual urine. Roentgenograms revealed a large shadow in the region of the gallbladder. Roent-

genograms of the stomach, kidneys, ureters, and bladder were negative. The Wassermann test on the blood was negative; the blood urea was 30 mg. for each 100 c.c.; the phenolsulphonephthalein test was 40 per cent. A small trace of albumin, a few erythrocytes, and 5 pus cells to the high-power field were found in the urine. The hemoglobin was 106 per cent by the acid hematin method; erythrocytes numbered 6,920,000 and the leukocytes 17,000; the differential count showed lymphocytes 28 per cent, large mononuclears 1 per cent, transitionals 2 per cent, neutrophils 67.5 per cent, and eosinophils 1.5 per cent. The total blood volume was 6,490 c.c., or 72 c.c. for each kilogram of body weight, and the cell volume by the hematocrit was 47 per cent. A diagnosis was made of essential hypertension of the benign type with arteriosclerosis, cardiac hypertrophy, relative polycythemia, cholelithiasis, obesity, and hypertrophy of the prostate.

There was evidence of definite arteriosclerosis in this case. Because of the increase in the number of erythrocytes and slight increase in hemoglobin, blood volume determinations were made. The obesity explains the relative decreased volume of blood. If the patient had been of normal weight, the blood volume would have shown normal values. There was no evidence of true polycythemia vera, nor did the symptoms or the patient's appearance suggest this. The combination of hypertension and the relative increase in erythrocytes suggest Geisbock's syndrome or polycythemia hypertonica. There was no evidence of pulmonary or cardiac disease to produce a compensatory increase in the relative number of erythrocytes. Dehydration disturbances were not present.

COMMENT

In the literature there has not been a sufficient number of cases of polycythemia with hypertension to permit definitely positive statements concerning this condition as a definite clinical entity. Cases of this type should be carefully observed for a long time. The blood volume should be studied if possible. The cases represent an interesting group of which little is known. Parkes-Weber is of the opinion that when this type of blood response occurs during the course of essential hypertension a better prognosis is justified. He believes that the condition of the blood is only transitory, and that the number of cells returns to normal.

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CYANOSIS

GEORGE R. CONSTAM AND GEORGE E. BROWN

THE bluish color of the skin of the mucous membranes and frequently of the viscera characteristic of cyanosis is due to the portion of the hemoglobin which is not in the state of oxyhemoglobin, but is present as reduced hemoglobin, methemoglobin or sulphhemoglobin. The intensity of the cyanosis depends on the absolute concentration of the volume of the reduced hemoglobin in the blood. Lundsgaard and Van Slyke have called attention to the six factors that modify greatly the clinical manifestations of the condition. They are (1) thickness of the skin, (2) pigment content of the skin, (3) color of the blood plasma, (4) concentration of hemoglobin in the blood, (5) quantitative exposure of the capillary blood, which is determined by the number, width, and length of the blood-filled capillaries and superficial venules, as has been shown quantitatively by Brown and Sheard, and (6) the degree of relative venosity or the amount of reduced hemoglobin in the capillary blood.

Since cyanosis is dependent on the disturbance of the oxygen-carrying function of the hemoglobin, a summary of the normal cycle of changes will perhaps aid in differentiating the pathologic variations. Normally the blood, in passing through the pulmonary capillaries takes up oxygen, and the hemoglobin is converted to oxyhemoglobin. The arterial blood usually does not take up its full quota of oxygen in the lungs. The average oxygen capacity of the blood of normal persons is 20.8 volumes per cent, and the blood in passing through the lungs will usually take up about 95 per cent of its quota of oxygen, and the arterial blood will have a saturation of 19 volumes per cent. The blood does not give up oxygen in its passage through the arteries, but during its passage through the tissue capillaries a portion of

the oxygen is used by the tissue (approximately 5 volumes per cent, or 25 per cent). This leaves 14 volumes per cent, or 70 per cent saturation of oxygen in the venous blood. Since 1 c.c. of oxygen combines with 0.75 gm. of hemoglobin the 6 volumes per cent of oxygen utilized by the tissues would be equivalent to 4.5 gm. of reduced hemoglobin.

The blood of a normal person with an oxygen capacity of 20.8 volumes per cent will contain 15.6 gm. of hemoglobin for each 100 c.c. of blood. The determination of the oxygen capacity of the blood becomes an accurate measurement of the amount of hemoglobin and is used as a standard for this purpose. The venous blood contains less oxygen since a quota is used by the tissues. As stated, in a normal subject the venous blood contains approximately 14 volumes per cent of oxygen, or a saturation of 70 per cent.

It is difficult to determine the amount of oxygen present in the capillary blood since it is removed progressively as the blood flows through these vessels. Lundsgaard considers the mean oxygen saturation of the capillary blood as the mean of the oxygen content of the arterial and venous blood. In the normal subject the oxygen content of the capillary blood would be $\frac{19 + 14}{2} = 16.5$ volumes per cent, a saturation of 80 per cent. This is an oxygen unsaturation of 4.3 volumes per cent ($20.8 - 16.5$), which is a measure of the amount of reduced hemoglobin.

In applying these facts to the explanation of the clinical problems relating to cyanosis much becomes clear. Lundsgaard has shown that the capillary blood needs an oxygen unsaturation of 6 or 7 volumes per cent, or 5 gm. of reduced hemoglobin for each 100 c.c. of blood, to produce clinically evident cyanosis. In other words, the composition of the capillary blood more closely approaches that of venous than of arterial blood. Normally if the blood in the veins were visible through the tissues, cyanosis would be marked. Such a condition has been described, and a similar one noted in our cases. Given, then, capillary blood with oxygen unsaturation of from 6 to 7 volumes per cent, cyanosis exists, but is subject to the various modifying

factors previously noted. In a negro the clinical evidence of the cyanosis would be greatly modified. From a clinical standpoint cyanosis, or increased unsaturation of the capillary blood may be produced by different conditions. Four types are differentiated:

1. Cyanosis resulting from failure of the blood to be completely oxygenated in the passage through the lungs; this is observed in high altitudes with reduced percentage of oxygen in the inspired air, or in consequence of disease of the pulmonary alveoli retarding oxygen exchange, such as pneumonia and emphysema.

2. Mechanical or shunt-type of cyanosis, in which venous blood enters directly into the arterial circulation; this is observed in certain types of congenital heart disease.

3. The peripheral type of cyanosis may be divided into two forms (*a*) in which there is an abnormal amount of oxygen removed from the blood in the capillaries, due possibly to the increased rate of oxygen consumption or more commonly to decreased rate of flow of the capillary blood, with abnormal loss of oxygen; this condition is observed in venous stasis, in cardiac disease, and in vasomotor disturbances of a vasoconstrictor type, such as Raynaud's disease, acrocyanosis, and exposure to cold, and (*b*) in which there is abnormal exposure or visibility of the venous blood.

4. A portion of the hemoglobin in the blood is in the form of methemoglobin or sulphemoglobin, the oxygen-carrying capacity of the hemoglobin is reduced, and the unsaturation of the arterial blood thereby reduced.

Types 1, 2, and 4 show diminished oxygen saturation or increased unsaturation of the arterial blood, as determined by samples obtained by arterial puncture.

Cyanosis is an important clinical sign. Its presence and intensity should be carefully noted from day to day. Quantitative determinations of cyanosis from the standpoint of color have been made by means of the Munsell color disks by Flagg, and spectrophotometrically by Sheard and Brown. Frequently cyanosis exists without producing symptoms. In order to illus-

trate the clinical application of the newer physiologic concepts in the study of individual cases, five illustrative cases of cyanosis are presented:

PULMONARY TUBERCULOSIS, CHRONIC BRONCHITIS, EMPHYSEMA, AND CYANOSIS OF PULMONARY ORIGIN

Case 1.—A retired farmer aged sixty-eight came to the Clinic in September, 1924 complaining of shortness of breath and cough, of about four years' duration. He had lost 8 kg. in weight. Severe dyspnea, brought on by the slightest exertion, prevented him from working. He was subject to colds, but most of the time cough was unproductive, dry, and very fatiguing.

The patient was undernourished and markedly cyanosed. The thorax was barrel-shaped and rigid. Respiration was difficult, the accessory muscles of the neck all being brought into action. The whole chest was hyperresonant to percussion. Vocal fremitus and vocal resonance were increased over both apices. Except for the apical regions, where expiration was prolonged and bronchial in character, breath sounds were normal. Both lungs seemed to be filled with moist, nonconsonant, medium-sized râles. A roentgenogram showed rather dense infiltrations of both apices. Bacilli of tuberculosis could not be recovered from the sputum on repeated examinations. There were no signs of cardiac lesion. The pulse rate was 78, the systolic blood pressure 124 and the diastolic 64. The walls of both radial arteries were markedly hardened. Neither the spleen nor the liver was enlarged. Teeth and tonsils showed signs of infection; both inguinal rings were relaxed; the presence of external hemorrhoids and moderate enlargement of the prostate were noted. The hemoglobin determined by the oxygen capacity was 16.1 gm., or 103 per cent. The erythrocytes numbered 4,000,000 and leukocytes 8,200. The hematocrit readings were 65 per cent plasma and 35 per cent corpuscles. The plasma volume, measured by the dye method, was 3,560 c.c., or 66 c.c. for each kilogram of body weight. The total blood volume was 5,519 c.c., or 102 c.c. for each kilogram of body weight. Gas analysis gave the following results:

Blood	Oxygen capacity, volumes per cent.	Oxygen content, volumes per cent.	Oxygen saturation, per cent.	Oxygen unsaturation volumes per cent.
Arterial	21.6	18.0	83.5	3.6
Venous		6.5	30.0	15.1
	Oxygen utilization	11.5		

Mean capillary oxygen unsaturation, 9.3 volumes per cent.

A diagnosis was made of bilateral pulmonary tuberculosis, emphysema, chronic bronchitis, benign hypertrophy of the prostate, and external hemorrhoids.

Two factors were seemingly responsible for the cyanosis in this case: (1) incomplete oxygenation of the arterial blood, as shown by increased oxygen unsaturation, due to the pul-

monary condition, and (2) increased oxygen utilization, indicating that an abnormal amount of oxygen was taken out of the capillary blood by the tissues. This is probably the result of slowing of the flow through the capillaries, due to increased venous pressure. The mean unsaturation of the capillary blood of 9.3 volumes per cent of oxygen, or 6.9 gm. of reduced hemoglobin, is more than the amount necessary to produce cyanosis. The low saturation of oxygen in the arterial blood is probably a factor in the production of dyspnea, as almost a fifth of the hemoglobin is not available for carrying oxygen. The increase in the volume of blood is probably compensatory in response to increased needs for oxygen.*

MYOCARDIAL INSUFFICIENCY WITH EARLY CHRONIC PASSIVE CONGESTION, GENERALIZED TELANGIECTASIA, AND CYANOSIS OF PERIPHERAL ORIGIN

Case 2.—A woman aged twenty-seven came to the Clinic in March, 1926 complaining of fatigue, shortness of breath, bluish-red discoloration of the skin, and nervousness. She had had scarlet fever and pneumonia in early childhood, pleurisy in 1914, typhoid fever in 1918, and tonsillitis in 1922. She had had one normal delivery; there had been no miscarriages. In September, 1924, while she was feeling in perfect health, she motored to Pike's Peak (altitude 14,000 feet). On the summit she suddenly complained of general malaise, shortness of breath, and noticed that the distal part of her legs and arms started to become blue and blotchy. She left the top of the mountain within an hour and the dyspnea diminished, but never disappeared completely. The discoloration of the skin progressed gradually, and in about four weeks affected the entire body. Since then the condition had remained stationary. The lower parts of the legs became slightly edematous when the patient walked; the edema shifted to the trunk on rest in bed. The patient noticed swelling of the cervical and inguinal lymph nodes. She was sensitive to heat and was particularly nervous on hot days. Menstruation became irregular, more profuse, contained clots, and lasted from six to seven days. For a year before admission severe nosebleed had occurred. She complained also of a dull aching pain in the back of the head and along the dorsal spine. In two years she had lost 12 kg. in weight. Several attacks of severe abdominal pain, associated with vomiting, had resulted in a diagnosis of appendicitis, but operation had not been performed.

The patient was very weak. The temperature varied from 98° to 99.6° F. She was comfortable while at rest, but the slightest exertion produced

*The normal mean value for blood volume, according to the dye method, is 89 ± 0.1 c.c. and for plasma volume 50 ± 0.2 c.c. for each kilogram of body weight.

marked dyspnea. The lips were cyanotic and the face bluish. The skin of the whole body was bluish-red and irregularly blotched, interspersed with persistent white areas particularly marked in the dependent parts of the breasts, the lower part of the abdomen, the legs, and the back. The discoloration disappeared on pressure, and to some extent also on elevation. There was considerable cyanosis of the nails of the fingers and toes, which showed a tendency to clubbing. The pupils were equal, regular, and reacted well to light and accommodation. The sclerotics were clear, the conjunctivæ were of normal color. There was some engorgement of the retinal veins. The ears, nose, and throat were normal. The oral mucosa and the tongue appeared deep red. The teeth were in good condition and of normal configuration. Enlarged lymph nodes, rather soft and not tender, were felt on both sides of the neck in the axillæ, the cubital fossæ and the inguinal regions. Systolic pulsations were visible in the supraclavicular fossæ on both sides. The right lobe of the thyroid gland was slightly enlarged.

The respiratory rate was 28. The lower borders of both lungs moved with deep respiration. There was some dullness in the left apex and in both bases. Fine crepitations could be heard in both lobes posteriorly. Roentgenograms of the chest revealed bilateral bronchiectasis. The vital capacity was 2,018 c.c. (normal about 3,000 c.c.). The sputum contained fusiform bacilli and spirilla. The heart dullness measured 11.5 cm. to the left and 6 cm. to the right of the median line in the sixth interspace. The apex beat was palpable in the fifth interspace, 10.5 cm. from the median line. No abnormal pulsations or thrills were seen or felt in the precordial region. The heart action was regular and rapid; the pulse rate varied from 80 to 110. The sounds were loud, with an inconstant systolic murmur best heard in the third and fourth left interspaces, parasternally, but transmitted over the entire precordium. The edge of the liver was felt 7 cm. below the costal margin in the right median clavicular line. The spleen and kidneys were not palpable. An electrocardiographic tracing showed sinus tachycardia, right ventricular preponderance, and inversion of the T-waves in all three leads.

The blood pressure was 132 and 90. The venous pressure measured by the Hooker method in recumbent position, hand at heart level, was 9.6 mm.; in sitting position, hand on heart level, 10.2 mm., in standing position, hand at heart level 12.8 mm.; on standing but hand lowered, 14.7 cm. of water. There were 15.5 gm. hemoglobin* for each 100 c.c. of blood, or 99 per cent hemoglobin. Erythrocytes numbered 4,800,000 and leukocytes 14,000. A differential count showed 32.5 per cent lymphocytes, 1 per cent large mononuclears, 2.5 per cent transitionals, 58 per cent neutrophils, 4 per cent eosinophils, and 2 per cent basophils. Two per cent of the red cells were reticulated. Hematocrit readings showed 52 per cent plasma and 48 per cent corpuscles. The volume index was 1.21. The total plasma volume was 3,790 c.c. or 50 c.c. for each kilogram of body weight. The whole blood volume was 7,300 c.c. or 114 c.c. for each kilogram of body weight. The relative blood viscosity was 6.3. Repeated urinalyses and phenolsulphonephthalein tests for renal

* 15.6 gm. of hemoglobin for each 100 c.c. of blood is taken as the normal standard for both sexes (Haden's standard).

function were negative. The blood urea and uric acid showed normal values. Pelvic and routine neurologic examinations were negative.

No methemoglobin or sulphhemoglobin could be found in the blood. Several blood Wassermann tests were negative. The gas analysis of the blood taken after one hour of rest in the recumbent position was as follows:

Blood.	Oxygen capacity, volumes per cent.	Oxygen content, volumes per cent.	Oxygen saturation, per cent.	Oxygen unsaturation, volumes per cent.	Mean capillary oxygen unsaturation, volumes per cent.	Oxygen utilization, volumes per cent.
Arterial	20.6	19.2	93.2	1.4		
Venous						
Arm at heart level		16.8	81.6	3.8	2.6	2.4
Arm elevated		10.8	52.0	9.8	5.6	8.4
Arm lowered		15.6	75.7	5.0	3.2	3.6

When the arm was raised for five minutes the blood taken from the basilic vein contained 10.8 volumes per cent oxygen as compared to 15.6 vol-

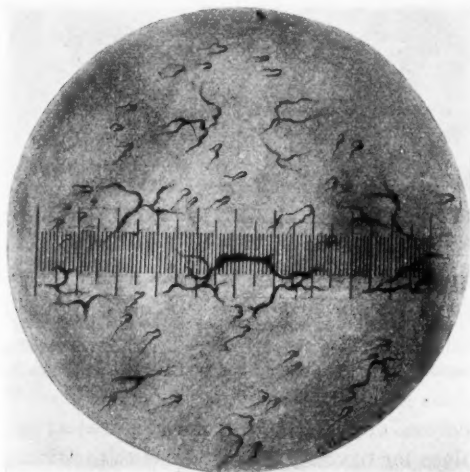


Fig. 267.—Skin capillaries and venules of the forearm in diffuse telangiectasis.

umes per cent oxygen content of the blood which was taken after the arm had been lowered for five minutes. Examination of the skin of the forearm, kept at heart level over a blue telangiectatic area, with the capillary microscope (Fig. 267), showed increase in number and size of dilated surface vessels and capillaries for each unit of skin surface. This explains the local-

ized areas of cyanosis. The histologic examination of an excised lymph node showed inflammation. Sections of the skin showed dilatation of the superficial capillaries (Fig. 268).

Digitalis had no effect on the condition. Oxygen inhalations relieved the patient and controlled the dyspnea, but the color of the skin remained unchanged. The skin temperature rose 1.4°C . as measured with the electrothermocouple. This disappeared, however, as soon as administration of oxygen was discontinued.



Fig. 268.—Dilatation of the superficial capillaries in a section of skin.

April 20 the patient was obliged to leave the hospital. Her home physician reported her condition in July as most pitiful, presenting a marked degree of anasarca. Repeated attempts to trace the case since have failed.

The analyses of the arterial blood collected at rest revealed normal values for oxygen content and unsaturation, indicating that the cyanosis was of peripheral origin. In 1925 Goldschmidt and Light described a case of local cyanosis as a result of injury to an ankle, in which no increase of oxygen unsaturation of the arterial blood was found and in which dilatation of the skin venules and capillaries was regarded as the primary cause for the discoloration of the skin. They substantiated this concep-

tion by investigations on local cyanosis produced experimentally in normal persons. The explanation for this form of cyanosis would indicate that this is not true cyanosis of the capillary blood, since its mean oxygen unsaturation was less than the threshold value for cyanosis. The cyanosis is due to abnormally large exposure of the venous blood through the dilated capillaries and venules. The lack of response to oxygen inhalations would support this conception. The condition of the blood is similar to that found in some cases of cardiac decompensation with edema and pulmonary stasis; that is, moderate increase in the circulating volumes of blood and plasma according to body weight, with increase in the percentage of cells by the hematocrit.

Diffuse telangiectasis is sometimes attributed to syphilis. Becker and others, however, found it frequently associated with cardiovascular renal disease and unrelated to syphilis. Neither in the history nor on examination did we find any signs of acquired or hereditary syphilis. Polycythemia vera was also considered, but the slight increase in the number of erythrocytes and volume of blood, and the absence of splenic enlargement eliminated this diagnosis. Furthermore, it would not explain the adenopathy and the pulmonary conditions. Certain features suggested right ventricular insufficiency due to compression of the pulmonary artery by enlarged nodes at the hilum of the lungs. Luthembacher reported a similar case of insufficiency as the result of the constriction of the left branch of the pulmonary artery, without dilatation of the proximal part of this vessel, by metastasis in the hilum from primary carcinoma of the lung. A similar affection might explain our case, including the generalized adenopathy present. The heart configuration typical for right ventricular affections (Posselt, Giroux, Largeau, Eppinger, and others) was not found on roentgen-ray examination; however, this had to be made in the recumbent position because of the weakness of the patient. Right ventricular insufficiency secondary to pulmonary arteriosclerosis or syphilis (Ayerza's disease) or pleuropericardial adhesions, congenital heart disease and myocarditis, involving mainly the right side of the heart (Paisseau, Oury, and Hamburger) were also taken

into consideration and apparently eliminated. Although we are unable to make an entirely satisfactory diagnosis, we present this case as a problem for diagnosis, in which many of the newer methods of investigation were necessary in attempting to interpret the nature of the disturbance.

POLYCYTHEMIA VERA

Case 3.—A Swedish farmer aged forty-two came to the Clinic in March, 1924 because of weakness, shortness of breath, and dizziness. He had had typhoid fever at fifteen, pneumonia at twenty, and influenza six years previously. Varicose veins had been present for more than ten years, the ulcers healing slowly at various times. His face had been red for several years; during the last twelve months this had become decidedly worse. Weakness, dyspnea on exertion, headaches, and dizziness had developed gradually within the last two years. For several months he had been unfit for any physical work. Extreme cold and heat were less and less tolerated, and sweating had become marked within the last nine months. Increasing nervousness accompanied these symptoms.

Examination showed a well-developed man of normal weight. His temperature was 97° F. The exposed parts of the body and the mucous membranes were very red, but lips and hands were distinctly cyanotic. Marked bilateral varicoseles and varicose veins were present. Observation of the nail-fold capillaries with the capillary microscope showed a slow but uniform flow through well-filled loops with marked engorgement on the venous side. Also the retinal veins appeared engorged; they were very dark and tortuous. The lungs were normal. Roentgenograms of the chest showed a slight degree of peribronchial thickening in both upper lobes. The heart was not enlarged. The reduplication of the first sound at the apex disappeared with exercise, the sounds at the base were rather distant. The pulse rate was 60, the blood pressure 135 and 98. The splenic border was felt 3 cm. below the left costal margin. The liver was not palpable. Urinalysis revealed the presence of a moderate amount of albumin, of traces of urobilin and urobilinogen, and a few hyaline casts and pus cells. A phenolsulphonephthalein test gave a return of 50 per cent within two hours after intramuscular injection. The basal metabolic rate was +5. The blood Wassermann test was negative. The hemoglobin determined by the oxygen capacity method was 151 per cent. Erythrocytes numbered 8,000,000 with 1.2 per cent reticulated cells and slight polychromatophilia; the leukocytes numbered 9,000, and the differential count showed lymphocytes 13 per cent, large mononuclears 0.5 per cent, transitionals 1 per cent, neutrophils 82 per cent, eosinophils 1.5 per cent, and basophils 2 per cent. The relative blood viscosity was 12, the coagulation time (Bogg), four minutes, the bleeding time three minutes. Hematocrit readings were 67 per cent corpuscles and 33 per cent plasma. The plasma volume measured by the dye method gave 3,750 c.c., or 46 c.c. for each kilogram of body weight. The total blood volume was 11,370 c.c., or 140 c.c. for each kilogram of body weight. Gas analysis gave the following results:

Blood.	Oxygen capacity, volumes per cent.	Oxygen content, volumes per cent.	Oxygen saturation, per cent.	Oxygen unsaturation, volumes per cent.
Arterial.	31.4	30.9	98.4	0.5
Venous		21.8	69.4	9.6
	Oxygen utilization	9.1		

The clinical diagnosis was polycythemia vera.

In order to stress the redness which is characteristic of the color of the skin in polycythemia vera, the term erythrosis is used in contradistinction to cyanosis. The difference between erythrosis and cyanosis is not conspicuous, and it is not surprising that cyanosis is frequently regarded as a symptom of polycythemia vera. According to Lundsgaard and Van Slyke, there are two reasons for this: the increased amount of hemoglobin in the blood, thus magnifying the color, and the increased exposure of capillary and venous blood due to a greater number of and larger capillaries. Our studies in cases of polycythemia have shown an additional factor of stasis, due probably to the increased viscosity of the blood and engorgement of the vessels. In visualizing the flow of the blood in the capillaries by the Lombard method, it is apparent that the color of the capillary blood is close to that in cyanosis. Slight decreases in the environmental temperature cause further slowing or complete stasis of the flow with evident cyanosis. The presence or absence of cyanosis in polycythemia vera is dependent in a large degree on the environmental temperature. The high oxygen utilization value is an evidence of peripheral stasis. In view of the high venous unsaturation and of the engorgement of the venous limb of the capillary loops, we hesitate to apply the usual mode of calculating the mean oxygen unsaturation of the capillary blood to this case.

METHEMOGLOBINEMIA

Case 4.—A woman aged forty-six came to the Clinic in June, 1920 complaining of cyanosis, dyspnea on exertion, and exhaustion. She had had migraine all her life and had used bromoselzer (acetanilid) for about fifteen years, as often as three times a week. Cyanosis of lips and finger tips, and dyspnea on exertion had developed about four years previous to admission. This condition was gradually becoming worse. Examination revealed marked cyanosis. Except for mild tachycardia (rate 100) there were no signs of

cardiac disorder. The blood pressure was normal. Hemoglobin (Dare) was 65 per cent, the erythrocyte count was 4,000,000; the leukocyte and differential counts were normal. Blood gas analysis was not undertaken. Spectroscopic examination of the blood demonstrated the presence of methemoglobin. An attempt to demonstrate this substance in the urine failed. The clinical diagnosis was migraine and methemoglobinemia, the latter due to acetanilid poisoning.

Cyanosis due to methemoglobinemia is sometimes found if patients use anilin derivatives in large amounts. Bromoselzer, containing acetanilid (antifebrin) is probably the one most commonly encountered. Acetphenetidin (phenacetin) is rarely used in sufficiently large quantities. It is said that other types of drugs, such as sulphonal, trional, veronal, potassium chlorate, and nitrates, also induce methemoglobinemia.⁸ The high incidence of migraine and the universal use of the anilin analgesic drugs would lead one to believe that there are many cases of undetected methemoglobinemia. Cyanosis and dyspnea in patients with history of attacks of migraine should raise the suspicion of the excessive use of acetanilid-containing drugs. Dyspnea, in the presence of cyanosis, suggests a cardiac disturbance. As cardiac disease was not found, it may be explained by the reduction in the proportion of hemoglobin available for oxygen-carrying purposes.

SULPHEMOGLOBINEMIA

Case 5.—A photographer aged forty came to the Clinic in June, 1927 complaining of stomach trouble of several years' duration; the history suggested peptic ulcer. He had suffered from headaches since childhood, and had used acetanilid for relief during the last nineteen years, at first intermittently but for the last two years constantly, about 20 grains (1.3 gm.) daily.

The patient's ash-gray complexion was contrasted with the cyanotic discoloration of the lips, mucous membranes, and finger nails. The temperature, pulse rate, and blood pressure were normal. No signs of pulmonary or cardiac disease could be elicited. Slight tenderness on pressure in the right epigastrium was attributed to duodenal ulcer, which was shown roentgenologically. Gastric analysis showed total acidity 60, and free acidity 44. Neither liver nor spleen was palpable. Tests of hepatic function (Rowntree-Rosenthal method) did not show dye retention, the blood serum gave an indirect van den Bergh reaction only. The serum bilirubin was estimated at 0.8 mg. for each 100 c.c. Repeated urinalyses were negative. The hemo-

globin value by the acid hematin method was 14.8 gm. or 95 per cent, and the erythrocytes numbered 4,000,000. The hematocrit values were 59 per cent plasma and 41 per cent cells. The total plasma volume, determined by the dye method, was 3,390 c.c., or 52 c.c. for each kilogram of body weight; the total blood volume was 5,750 c.c., or 89 c.c. for each kilogram of body weight. The leukocytes numbered 9,500; the differential count showed normal values, and the structure of the cells was as usual. The Wassermann test on the blood was negative. Gas studies of the venous blood gave the following values:

Oxygen capacity, volumes per cent.	Oxygen content, volumes per cent.	Oxygen saturation, per cent.	Oxygen unsaturation, volumes per cent.
17.2	6.6	33.4	13.2

Spectroscopic examination revealed the presence of sulphhemoglobin in the blood.

If the 14.8 gm. of hemoglobin had been derived from normal hemoglobin, the oxygen capacity of the latter would amount to 19.8 volumes per cent. The directly measured oxygen capacity of the blood was only 17.2 volumes per cent. A certain part of the hemoglobin, the sulphhemoglobin, did not combine with oxygen. The hemoglobin value determined by the acid hematin method includes all forms of hemoglobin, irrespective of its faculty to carry oxygen. The oxygen capacity method, however, determines merely the amount of oxyhemoglobin. The difference between the two values represents the loss of oxygen-carrying power as a result of the formation of sulphhemoglobin. The oxygen capacity, calculated from acid hematin hemoglobin value, is 19.8 volumes per cent; the oxygen capacity measured directly equals 17.2 volumes per cent; the difference is 2.6.

It is self-evident that for the calculation of the venous oxygen saturation and unsaturation, the oxygen capacity, which includes the sulphhemoglobin value, has to be used. Accordingly the value in this case was 19.8 volumes per cent, minus 6.6 volumes per cent, equalling 13.2 volumes per cent venous oxygen unsaturation.

In 1902 Stokvis and Talma, independent of each other, described an enterogenous type of cyanosis in cases of enteritis and demonstrated the presence of methemoglobin in the blood. In 1904 van den Bergh, in a similar case, found the hemoglobin of the erythrocytes partly transformed into sulphhemoglobin. Sulphhemoglobinemia was attributed to increased intestinal putre-

faction by some authors. However, there were cases in which they were unable to demonstrate an augmentation in the absorption of hydrogen sulphid. Experiments *in vitro* showed that when the blood is exposed to hydrogen sulphid a rather large quantity of the latter is necessary for the formation of sulphhemoglobin. Adding a reducing substance seems to sensitize the blood to the action of the hydrogen sulphid and facilitates this process considerably. Snapper, who observed two cases of sulphhemoglobinemia after the prolonged use of acetphenetidin (phenacetin), considered the anilin derivative as the factor which sensitized the hemoglobin of the red blood corpuscles to the action of the hydrogen sulphid. He produced sulphhemoglobinemia ex-

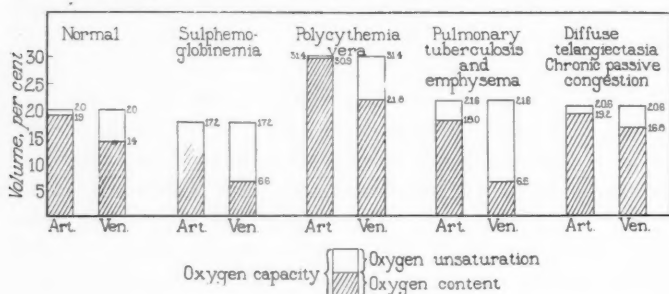


Fig. 269.—Blood gas analyses.

perimentally by feeding phenacetin in moderate doses, together with small amounts of precipitated sulphur or eggs. Both an active resorption of hydrogen sulphid and the presence of a sensitizing factor, such as an anilin derivative, seemed to be necessary for the production of sulphhemoglobinemia. The combination of chronic constipation, or the ingestion of sulphur-containing foods, with the prolonged use of acetanilid could be considered the cause of the sulphhemoglobinemia in this case.

The results of the blood gas analyses in the second, third, fourth, and fifth cases are diagrammatically presented in Fig. 269. Each column represents the total oxygen capacity of the blood: its black part the actual oxygen content, its white part the oxygen unsaturation. The oxygen utilization in the tissues

is expressed by the difference in height between the black parts of the two corresponding columns.

The oxygen content of the arterial blood was not determined in the case of sulphhemoglobinemia. The increase in venous oxygen unsaturation is very conspicuous. This, we believe, is due to an increased unsaturation of the arterial blood due to loss of oxygen-carrying hemoglobin. The oxygen capacity in the blood in the case of polycythemia vera is much increased, indicating a high value for the hemoglobin. The utilization value for oxygen is increased, indicating stasis. The augmentation in the oxygen unsaturation of the arterial and venous blood in Case 1 is quite marked. Normal values for the oxygen content, and unsaturation of the arterial blood, and oxygen utilization were present in the case of diffuse telangiectasis with myocardial insufficiency, indicating a peripheral type of cyanosis due to abnormal exposure of the normal venous blood.

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RECURRENT IDIOPATHIC SUPERFICIAL PHLEBITIS: ITS SIGNIFICANCE IN ADULT MEN

WALTER R. JOHNSON

SUPERFICIAL phlebitis is not at all rare. In cases in which a fairly definite cause can be adduced (recent infection, as typhoid fever, influenza or pneumonia, recent operation, local inflammation with extension to a vein, definite varicosities, or the coexistence of polycythemia) palliative treatment such as hot packs and rest in bed is, perhaps, adequate and a more rigid investigation need not be made. When, however, superficial phlebitis occurs in an otherwise healthy adult man the medical advisor must be on his guard. Besides the usual treatment, he must institute careful inquiry into the past history to determine, if possible, the existence of previous phlebitis; he must carefully locate, palpate, and record the presence or absence of pulsations in the main arteries of the extremities, and he must determine roughly the circulatory efficiency of these vessels by observing the appearance of the extremities when elevated and when dependent. These studies are indispensable if a proper evaluation of the significance of the phlebitis is to be attempted.

As has been shown repeatedly by Buerger and others, wandering and recurrent superficial phlebitis is frequently the first subjective and objective evidence of a more serious underlying disease process, thrombo-angiitis obliterans, or Buerger's disease. If such condition is present it is of the utmost importance to recognize it early and warn the patient so that adequate control measures may be instituted before frank arterial insufficiency develops. Even in cases in which there are no signs of arterial involvement, it is well to remember that idiopathic superficial

phlebitis may precede by months or years the first evidences of obstructive arterial disease. If these precautions are followed, many cases of terminal thrombo-angiitis obliterans with gangrenous extremities, intolerable pain, and total incapacitation may be prevented.

Case 1. Typical thrombo-angiitis obliterans; arterial disease in the left leg and superficial venous thrombosis in the right.—A man aged forty-six (Gentile) came to the Clinic July 8, 1926 because of an inflammatory process in the right thigh. The patient owned a garage, and spent much of his time on the cold damp concrete floor of the repair room. He was a heavy smoker, averaging two to three packages of cigarettes, a few cigars, and an occasional pipeful each day since the age of fifteen. About six years previously he had noted fatigue and cramp-like pain in the arch of the left foot after unusually strenuous exercise, such as trout fishing or elk hunting. A rest of a few minutes would restore him to normal and he could continue the task in hand with perfect comfort until arch claudication again forced him to stop. Gradually his tolerance for exercise decreased so that two years after the onset of the trouble a brisk walk of five or six blocks would invariably induce severe cramp-like pain in the foot and calf of the left leg. If he walked slowly he could travel double this distance without distress. At about this same time a tender, inflamed streak developed along the mesial tibial border of the previously healthy right leg. A firm, tender, cord-like mass was distinctly palpable beneath the inflamed skin. He consulted a physician who diagnosed phlebitis and prescribed salicylates. The phlebitis cleared promptly. During the third winter of the disease unnatural coldness of the left foot led him to wear heavy woolen socks, which he had never done before. Even with the coming of warm weather he found it necessary to retain the wool covering. During the same winter he began to suffer from night pains and cramps in the left foot and calf. The pains were sufficiently severe to awaken him from sleep and force him to walk about the room; they had recurred each winter until shortly before admission. Four years after the onset of the first symptoms the toes of the left foot became dusky reddish-blue when dependent. By this time, too, he was unable to walk more than 50 yards without foot and calf claudication. About six weeks before admission a painful, inflamed, and tender cord-like mass appeared at the mesial border of the right tibia. The process extended upward slowly and as it did so it cleared below, leaving a brownish streak of pigmentation along the course of the saphenous vein. The inflamed vein was slightly painful, but did not prevent walking. It was decidedly tender to pressure. At the time of admission the left leg had improved somewhat and he could walk a block before claudication occurred. There was no pain in the right leg except that caused by the active phlebitis.

The general examination was essentially negative except for slight pyorrhea, one apically infected tooth, and a tiny fecal fistula in an old appendectomy scar. The right thigh presented an inflamed streak of skin along

the course of the saphenous vein (Fig. 270). The vein itself was palpable as a tender, cord-like mass to within 10 cm. of the pubic tubercle. The acute inflammatory process ceased in the lower third of the thigh, but the vein could easily be palpated below the knee where dusky brownish pigmentation of the skin signified the presence of recent phlebitis. All the arteries in the right leg pulsated normally, the foot was flushed and warm, and on elevation there was no pallor. There was distinct rubor of the toes of the left foot and the foot was icy cold to touch. Vessels could not be felt below the popliteal space. On elevation the whole foot became cadaverous and on dependence a slow but marked reactionary rubor of the toes and instep succeeded the pallor.

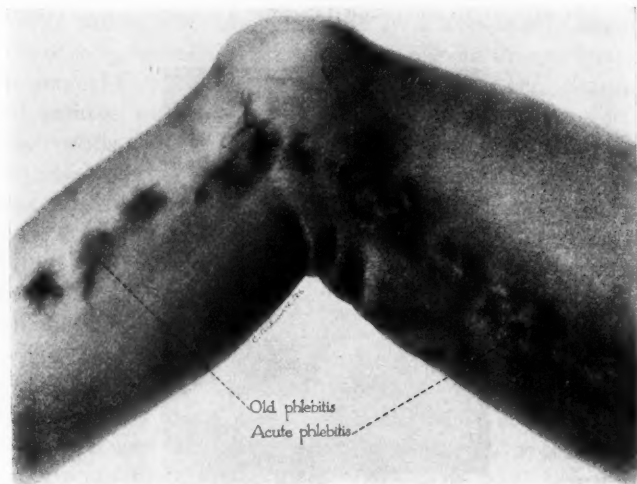


Fig. 270.—Superficial migrating phlebitis in case of Buerger's disease.

A diagnosis was made of thrombo-angiitis obliterans of both legs, fairly well compensated arterial lesion on the left, and a superficial migrating-phlebitis stage without apparent arterial involvement on the right. A portion of the thrombosed saphenous vein was removed and showed subacute thrombosis with beginning organization (Fig. 271).

This case is a clear-cut example of thrombo-angiitis obliterans (Buerger's disease). The features of particular interest and instructive value are: (1) the arterial disease was confined to the left side and the symptoms complained of in the left leg

were wholly arterial in nature; (2) the venous lesion remained localized to the right leg, and presented an entirely different set of symptoms; (3) the thrombotic process in the arteries of the left leg, after progressing slowly for four years, came to a spontaneous standstill, and (4) on the two occasions the patient consulted a physician, an attack of superficial, migrating phlebitis and not the arterial symptoms induced him to seek aid.

It may be noted that the first intimation of trouble with the feet occurred only after strenuous exercise and only in the left leg. The symptoms complained of were a sense of undue fatigue



Fig. 271.—Thrombus well organized. Newly formed vascular channels and collection of lymphocytes in thrombus and wall of vein. Clinically this vein was acutely involved; pathologically the process is subacute.

in the arch of the left foot, the fatigue rapidly giving way to actual severe cramping pain (intermittent claudication) similarly localized to the arch. Rest of a few minutes afforded complete relief and the patient was able to continue with perfect comfort until claudication again forced him to rest. These symptoms are absolutely pathognomonic of a deficient supply of arterial blood, and are due, as far as can be determined, to anoxemia or insufficient oxygenation of the affected parts. In this case such

symptoms occurred after exceptional strain had been put on the circulatory system, such as arduous wading in rocky mountain streams, and prolonged walking over rough, uneven ground. In ordinary life the demands of the tissues of the left foot for oxygen were easily met and consequently there were no symptoms. Had careful examination been carried out at the time claudication was first noted, the dorsalis pedis or post-tibial arteries (possibly both) would undoubtedly have been found greatly diminished in volume or even absent.

The patient was intelligent, and gave a clear-cut, definite story of the progression of symptoms, and one can almost visualize the gradual thrombosis of the arteries in the left leg. Starting first, perhaps, with obliteration of the dorsalis pedis and posterior tibial vessels and exercise cramps in the arch alone, the disease progressed slowly upward until, two years after the first symptoms, a brisk walk of five or six blocks would invariably induce severe cramping pains in both the foot and calf. The pain in the calf indicates that at this time the arteries supplying these muscles were affected and unable to perform their normal function, that is, adequate supply of oxygenated blood to the tissues. During the next two years the obliterative arterial process in the left leg gradually advanced. It became impossible to walk more than fifty yards without claudication. Then, for some unknown reason, the disease became nonprogressive; the symptoms instead of becoming more severe as is usual, remained unchanged for a time and then slowly began to improve until, at the time of admission, the patient was able to walk at least 100 yards before claudication pain enforced rest. This improvement is probably the result of nonprogression of the active thrombotic process within the arteries, and the development of a partially effective collateral circulation.

The symptoms from inflammation of a superficial vein are the same as those from inflammation in any situation: local swelling, heat, redness, and pain. The pain usually is dull and throbbing, particularly with the limb dependent. If the deeper veins chance to be simultaneously involved, the pain is usually more severe and a systemic reaction with malaise and fever

may obtain. There is never exercise pain; indeed exercise frequently reduces the soreness in the affected limb. The pain occurs at rest; this point is important. Ordinarily the patient describes the phlebitis as "little red, tender swellings in the skin," and denies marked spontaneous pain. Indeed, in many instances there is complete lack of subjective discomfort and the only complaint is recurring crops of "little red lumps," which may be slightly tender to pressure.

Case 1 affords an unusual opportunity to differentiate the symptoms of progressive arterial obstruction in one leg (the left) from those of the same process in the superficial veins on the opposite side. When the first attack of phlebitis occurred, the only symptoms noted by the patient were those of mild inflammation: local heat, redness, tenderness, slight swelling, and slight pain which was present at all times. Despite the fact that intermittent claudication had been manifest two years and was increasing in severity and in rapidity of onset after exercise, he had never consulted a physician, but when superficial phlebitis occurred in the previously healthy right leg he decided that he needed attention. It is a peculiar fact that many patients with Buerger's disease fail to seek aid until phlebitis occurs. The presence of an inflamed tender lump beneath the skin makes an impression which cannot be denied; the patient actually sees it, he feels of it and finds it tender, and then he concludes that medical opinion is desirable. Sometimes he will fail to volunteer a history of claudication (arterial symptom) but will refer all of his symptoms to the phlebitis. This point is important and shows the need for differentiating the symptoms of the two processes, which, although related, vary so markedly in their prognostic significance. A physician was consulted who, overlooking entirely the serious obstructive arterial lesion in the left leg, made a diagnosis of phlebitis in the right and prescribed salicylates. The inflammatory lesion of the vein cleared, of course, and did not recur until shortly before the patient's visit to the Clinic. Fortunately for the patient in this instance the arterial disease came to a spontaneous standstill two years later. That such spontaneous arrest occurs is well known and it lends

impetus to efforts toward earlier diagnosis and treatment. It tends also to dispel the hopeless gloom which ordinarily surrounds the victim of this disease; for if nature unaided can sometimes effect a "cure," why cannot nature with reasonably intelligent aid do even more? It is the hope of those who see Buerger's disease frequently that, as diagnoses are made earlier and appropriate treatment instituted before the advent of gangrene, there will be an increasing number of arrested cases. In all too many histories, however, there is a dreary repetition of mistaken or incomplete diagnoses, a pitiful succession of arch supports and other orthopedic appliances, and finally gangrene and amputation. If physicians would remember that superficial phlebitis in an otherwise healthy adult man is frequently the forerunner or objective evidence of a grave arterial lesion of the extremity, many amputations might be avoided.

Case 2. Thrombo-angiitis obliterans: phlebitis preceded the arterial symptoms by eleven years.—A man aged thirty-eight (Gentile) came to the Clinic February 17, 1924 because of eighteen years of recurrent attacks of painful red "welts" on the left foot, ankle, and calf. He was a draftsman by occupation and had smoked about 10 cigarettes daily for many years. For the first eleven years the individual attacks lasted but a few days and occasioned relatively little disability. During the succeeding seven years, however, they had become much more severe, with exquisitely tender red lumps persisting for about a week. There was dull throbbing pain in the leg in the dependent position. Attacks recurred at almost monthly intervals. For seven years he had noted, after a brisk walk of a few blocks, left calf claudication, relieved always by a few minutes of rest and recurring on resumption of exercise. More recently arch claudication in the right foot had obtained and he had become aware of coldness and numbness in both feet.

General examination showed definite rubor of the feet and on elevation marked pallor. Patches of brownish pigmentation were seen on the left foot, ankle, and calf. On palpation firm, cord-like masses were noted beneath the pigmented skin. The right dorsalis pedis artery was not found, but the posterior tibial and popliteal vessels seemed normal. On the left, no arteries could be found distal to the popliteal.

A diagnosis of thrombo-angiitis obliterans with recurrent superficial phlebitis was made. A section of thrombosed vein was removed and the same type of lesion found as in Case 1.

This case is of interest because of (1) the unusually long history of recurrent superficial phlebitis without evidence of ac-

companying arterial disease; (2) the severity of symptoms from the phlebitis, and (3) the slow progression of the thrombotic process in the arteries.

An eleven-year history of recurrent phlebitis without evidence of concomitant arterial involvement is decidedly unusual. In many instances the phlebitis precedes the arterial symptoms but shortly, and frequently a history of arch or calf claudication may be uncovered in the patient's first attack of phlebitis. A definite history of superficial thrombosis of the vein is obtained in less than a third of the cases of thrombo-angiitis obliterans. This may be due in part to the fact that the discomfort is often relatively slight, and may remain unnoticed if the symptoms from the arterial involvement are sufficiently severe. In hyposensitive persons, subjective discomfort related to the phlebitis may be entirely absent, but by careful questioning a story of recurrent attacks of reddish firm nodules along the course of the superficial veins may be elicited. In this case, the symptoms were so severe as to lead the attending physician to a diagnosis of recurrent rheumatic fever. However, the lack of systemic reaction, the absence of signs of endocardial involvement, the prolonged history, and the fact that the pain and tenderness were always localized to the little inflammatory lumps beneath the skin made such a diagnosis untenable. Erythema nodosum, too, had been suggested, but at this time definite claudication on exercise had obtained. Had attention been shifted to the arteries, a diagnosis of obstructing arterial disease would have been inevitable.

An eighteen-year history of thrombo-angiitis obliterans without gangrene is extremely uncommon, although, as more care is taken in prying into the past history of men complaining of pain in the legs on exercise, similar instances are sometimes uncovered. In some instances the disease progresses to a certain point and then apparently comes to a standstill, as occurred in Case 1, leaving the patient with a definite exercise limit beyond which he cannot go without claudication pain. With the development of collateral circulation, this limit is gradually extended. In most instances, however, there is a gradual

increase in the severity of the symptoms until finally gangrene supervenes. The average duration of the disease from first symptoms to gangrene is less than six years.

Case 3. Recurrent phlebitis in the left leg without evidence of concomitant arterial disease.—A man aged thirty-eight (Gentile) came to the Clinic, July 26, 1927 because of pain and swelling in the left leg. He was a salesman and had smoked heavily for many years. In October, 1925 he had been confined to bed for two weeks because of superficial soreness on the inner aspect of the left calf associated with general fever, local heat, and tenderness and swelling around the ankle. He recovered spontaneously and remained well until the spring of 1926 when a similar attack forced him to bed for three weeks. In July a third attack of the same trouble kept him from work four weeks. Following this he was well until January, 1927, when there was a fourth and more severe attack with edema, pain, and swelling along the course of the saphenous vein up to the groin, local tenderness and heat, and systemic fever. Between attacks the leg had been normal except for edema after long hours of work.

General examination disclosed slight pyorrhea, a slightly enlarged and tender prostate and prostatic infection, graded 3, but without significant cultural data. There was a firm tender cord along the course of the left internal saphenous vein to a point 5 cm. below Poupart's ligament. The lower part of the leg was moderately edematous and several small cord-like masses were palpable on the medial and lateral aspects of the calf. All of the palpable vessels of the extremities (brachial, radial, ulnar, femoral, popliteal, dorsalis pedis, and posterior tibial) were pulsating normally. Circulatory efficiency tests were negative and there were no trophic changes in either extremity.

A diagnosis of recurrent deep and superficial phlebitis of the left leg was made. It was thought wise to eradicate all traces of focal infection. Diseased tonsils had been removed six months previously. The pyorrhea and prostatitis were treated. Local treatment to the legs consisted of contrast baths, postural exercises, and local heat by means of a baking tent; these measures were to be followed at home.

Thrombo-angiitis obliterans was suspected in this case but, in the absence of demonstrable arterial involvement, the diagnosis could not be made. Microscopic sections of a portion of vein removed for culture and study showed organizing thrombophlebitis of an indeterminate type. The symptoms from the phlebitis, too, were more severe than are usually encountered in Buerger's disease. The patient was bedridden for weeks at a time because of the severe, constant pain in his leg. The involvement of the deeper veins was evidenced by the persistent

edema. In the absence of postural effects such edema is not a common event in Buerger's disease, at least not until the terminal stages are reached.

The precipitating cause of the four attacks of phlebitis could not be determined. The patient was of the opinion that trauma always preceded the infection, but this conclusion may have been influenced by the fact that he had a disability clause for accidents in his insurance policy. The apparently infectious nature of the whole disease process suggested the possibility that focal infection was responsible and the elimination of foci was advised on this basis.

Because of the indeterminate character of the complaint it was judged wise to treat it as a frank case of Buerger's disease, and consequently contrast baths, postural exercises and baking, measures designed to facilitate establishment of collateral circulation, were prescribed. This treatment was carried out at home one or more times daily as the occupation of the patient permitted. Ten months after dismissal from the hospital the patient was seen again. He had remained free from further trouble and, aside from the edema of the left leg, was quite comfortable. There was no evidence of arterial disease at this time.

There is, of course, no certainty that this patient will continue well. If the phlebitis was due to thrombo-angiitis obliterans, there is every reason to expect the development of arterial thrombosis later. Such an event is guarded against as effectively as possible by removal of evident foci of infection, by discouraging excessive use of tobacco, by teaching the patient a few fundamental principles in the hygiene of the feet, and by the use of heat, contrast baths, and postural exercises.

Case 4. Superficial migrating phlebitis without thrombosis: periphlebitic lymphangitis.—A farmer aged sixty-five came to the Clinic August 25, 1921 because of pain in the arms and legs. July 15 severe pain had occurred in the calf of the left leg, with localized swelling and inflammation. The condition improved slowly until August 19 when painful, localized areas of inflammatory swelling appeared along the course of the superficial veins of the forearm and both legs. The swelling was not associated with chills or

fever and, with the exception of a slight sore throat, there was no evidence of generalized infection. For two weeks before admission the patient had noticed that his feet were swollen and would pit on pressure. He lost 40 pounds in weight, and suffered from complete loss of appetite.

General examination revealed a somewhat emaciated, senile man, apparently quite ill. The temperature was 99° F., the pulse 90. There was moderate pyorrhea. Edema of the left foot was graded 2 and both femoral veins were tender to pressure. On the mesial aspect of the right knee was a reddened tender area where an apparently thrombosed saphenous vein could be felt. Similar tender cords were found in both forearms beneath the inflamed skin.

While in the hospital the patient seemed at first to improve. His temperature became normal and the local inflammatory processes subsided. September 3, however, he complained of abdominal distress aggravated by food and relieved by bowel movement. The abdomen was tense. Involvement of the abdominal veins was suspected. At the same time several new areas of acute inflammation appeared in the veins of the legs and arms, being in all instances located proximal to the area of vein last affected. With the appearance of each new focus, the temperature varied between 99° and 100° F. September 29 tenderness of the right external jugular vein developed. October 2 there was definite edema of the conjunctiva of the right eye, and the orbital tissues were inflamed. The edema about the eye cleared rapidly and improvement was gradual but continuous until the patient was dismissed October 7.

Treatment in the hospital consisted solely of local application of heat, absolute rest in bed, and forced feedings.

It was first thought that the patient was suffering from generalized thrombophlebitis. The acutely involved veins could easily be palpated; the inflammation advanced from a focus marked by a reddened area in the overlying skin and was indicated by a red streak, slight tenderness, and a slight amount of edema. However, as soon as the acute process had subsided the veins could no longer be palpated. When they were superficially located they could be stripped empty and then observed filling normally. From these signs it was apparent that thrombosis had not occurred and that the inflammation had in all probability not affected the intima.

An analogous case with similar development was reported by Northrup in 1896. The superficial veins in his case were unusually prominent and so lent themselves admirably to study. Northrup designates his case "periphlebitic lymphangitis," and said "infectious thrombophlebitis rarely, if ever, disappears completely, leaving a pervious vein." He postulated for this reason an inflammation of the lymphatic channels of the outer vessel coat, with lymphocytic infiltration and possibly edema accounting for the cord-like feel of the acutely involved vessel. Whether

or not this explanation is correct, certainly it explains adequately the disease picture seen in Case 4.

SUMMARY

Four cases of superficial phlebitis are presented. In the first two cases the diagnosis was missed because attention was confined to the inflamed veins. A serious arterial lesion was permitted to go undiagnosed and untreated for years, because the symptoms were not properly evaluated and the general examination did not include a careful study of the arteries. In the third case arterial involvement could not be demonstrated, but a presumptive diagnosis of thrombo-angiitis obliterans was made to safeguard the patient's future welfare. The fourth case indicates that phlebitis need not be accompanied by a thrombotic process, but that inflammation of the perivascular lymph channels may cause all the symptoms of thrombophlebitis except the thrombotic occlusion of the vessel.

A plea for more painstaking examination of the arteries in cases of idiopathic superficial phlebitis is made.

ACUTE RENAL INSUFFICIENCY FOLLOWING SURGICAL OPERATION FOR CARCINOMA OF THE SIGMOID AND RECTUM

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IN many cases of obstructive lesions in the upper gastrointestinal tract renal insufficiency has developed both before and after operation. In most instances the lesions are of such type that early recognition and proper treatment results practically in complete recovery. In the last two years we have not infrequently noted clinically that a similar type of acute renal insufficiency developed following operation for carcinoma of the lower part of the colon; toxic symptoms associated with oliguria were the reasons for further investigation of renal conditions. The patients appeared very ill; they were nauseated, and usually hiccupped. A certain degree of fever, the result of low-grade peritonitis, was always present. Mental confusion occurred in several cases; in one it progressed until the patient was in a comatose state (Case 1).

The important data as to impaired renal function were, chiefly, oliguria and elevation of blood urea. Urinalysis disclosed slight to moderate albuminuria with occasional casts and red blood corpuscles. The phenolsulphonephthalein excretion was impaired during the period of oliguria. The absence of hypertension, retinitis, or other cardiovascular signs was striking. Edema, when it occurred, always followed a large intake of fluid given to promote diuresis. In most cases diuresis was followed by complete restoration of renal function, but in some instances, in spite of improvement in renal excretion, death resulted from peritonitis or an associated infection. In no case in which adequate treatment was given did death result chiefly from failure of renal function. From this group we shall report

four cases. In none of these was pyelonephritis or cardiac decompensation the cause of the renal lesion.

REPORT OF CASES

Case 1.—A man aged fifty-one came to the Clinic October 26, 1926 because of previous attacks of diarrhea and recent gradually developing obstipation.

There was a palpable mass in the left lower quadrant of the abdomen. Roentgenograms of the sigmoid showed an intrinsic filling defect, and a diagnosis of carcinoma of the sigmoid was made. At this time renal function was apparently satisfactory. There were no symptoms of renal disease. The systolic blood pressure was 100, and the diastolic 68. Urinalysis was negative for albumin, casts, blood, or pus. There was practically no anemia. Estimations of blood urea, and phenolsulphonephthalein tests of renal function were not carried out.

November 4 a modified first stage of Mikulicz operation for perforating carcinoma of the sigmoid was performed. The surgeon felt that the growth could be removed satisfactorily but the perforating carcinoma had resulted in the formation of an abscess and this, of course, added to the risk of the operation. The pathologist reported annular adenocarcinoma, graded 3. The patient's convalescence was satisfactory for six days, and then severe toxic symptoms developed with hiccough which was difficult to control. Moderate fever and several slight chills occurred and there was some drainage from the abdominal wound. The lungs apparently were clear. He soon began to vomit, and the output of urine diminished. The blood urea rose from 22 mg. for each 100 c.c. of blood on the eighth day, to 34 mg. on the tenth day, to 120 mg. on the twelfth day, and to 200 mg. on the thirteenth day. During this period repeated washing of the stomach revealed only slight retention. The condition of the blood was not indicative of high intestinal obstruction, the plasma sodium chlorid and plasma carbon dioxid combining power being normal. The urine contained albumin, graded 1 or 2, a few red blood cells, and a few pus cells. The systolic blood pressure was 130, and the diastolic 80. With the rise in the blood urea toxemia became more marked; the patient was irrational, and on November 15 he was in coma. Respirations were shallow; the pulse rate was 104 each minute and irregular. There was a trace of edema in the face, a trace in the lumbosacral region, and a moderate amount in the lower part of the legs. The edema was probably the result of fluid intake which had been considerably higher than the fluid output for several days. Hypertonic solutions of glucose were given intravenously in conjunction with a fluid intake up to 3,000 c.c. daily. The output of urine increased somewhat and the blood urea dropped rapidly to 41 mg. for each 100 c.c. on the fifteenth day, but the edema and the fever persisted. In fact, the edema seemed to increase gradually. November 23 a red, fluctuating tender mass was noted in the right thigh. This was opened and drained, and the fever gradually diminished. At this time the blood urea was 22 mg. for each 100 c.c. The condition of the urine was unchanged and the blood pressure was normal, but there was marked edema. Fluids were then re-

duced; a fair volume of urine continued daily, and in a short time the edema had largely disappeared. December 3 the patient was practically free from edema. The urea, creatinin, fat, and cholesterol values in the blood were normal, and blood pressure was normal. Urinalysis showed albumin graded 2, and pus graded 2. January 7 urinalysis was negative except for a trace of albumin and thereafter renal function was normal, although the patient was in hospital for 147 days after the operation.

The patient was dismissed in good condition. He returned for a check-up examination September 22, 1927, at which time the blood pressure was 120 and 75. The blood urea was 30 mg. for each 100 c.c.; urinalysis was negative except for albumin, graded 1, and an occasional pus cell. The malignant growth had recurred. A course of roentgen-ray treatment was given and the patient allowed to return home October 14. We have not heard from him since.

Case 2.—A man aged sixty-four came to the Clinic October 10, 1927, presenting a history of carcinoma of the sigmoid of long duration. Two years previously a cecostomy had been performed elsewhere for partial obstruction. At this time the diagnosis of carcinoma of the sigmoid was made and the patient was told he had not long to live. However, he continued to be fairly well until two months before admission when he became markedly constipated with bloating and distress in the abdomen.

On examination he appeared to be in a fairly good general condition, considering his age and disability. He had lost 15 pounds since the operation two years previously, and was still somewhat obese. The hemoglobin was 70 per cent (Dare), erythrocytes numbered 4,640,000 and leukocytes 11,600. The Wassermann test on the blood was negative. Roentgenograms of the chest were negative. The heart was normal except for occasional extra systoles. The systolic blood pressure was 130, and the diastolic 80. Urinalysis was negative for albumin, casts, blood, and pus. Electrocardiograms, tests of blood urea and the phenolsulphonephthalein return were not made. Arteriosclerosis was marked, but symptoms of edema, dyspnea, or abnormalities of the cardiovascular and renal systems were not noted. Proctoscopic examination revealed carcinoma of the sigmoid about 25 cm. above the anus, measuring about 8 by 6 by 5 cm. The abdomen was markedly distended, and there were symptoms of partial obstruction.

Operation was performed October 17, 1927. An enormously distended colon, and double obstruction, one in the sigmoid due to carcinoma and another of a subacute nature at the splenic flexure from inflammatory adhesions, were found. The cecostomy opening was not functioning satisfactorily, and the large bowel was packed hard with feces. Resection from the middle of the transverse colon down to the middle of the sigmoid was performed. The operation was extremely difficult, and the immediate operative risk appeared very high. Convalescence was stormy beginning immediately after the operation. Following the intravenous injection of 10 per cent glucose solution a paroxysm of auricular fibrillation developed which lasted a little less than an hour. Tonic doses of digitalis were administered and the patient's condition was fairly satisfactory until the next day, although

the output of urine was beginning to diminish definitely. October 20, the fourth day after operation, another paroxysmal attack of auricular fibrillation occurred following the administration of glucose solution intravenously. By this time the output of urine was definitely diminished. October 21 only 310 c.c. of urine was voided on an intake of nearly 3,000 c.c. Urinalysis showed albuminuria, graded 1, a few hyaline casts, and an occasional pus cell. The blood urea was 70 mg. for each 100 c.c. Oliguria persisted the next day, during which time 800 c.c. of urine was voided on an intake of 2,700 c.c. Urinalysis, October 22, showed albuminuria, graded 2, and an occasional pus cell. The blood urea was 80 mg. for each 100 c.c. The fluid intake was kept between 2,500 and 3,000 c.c. daily and in the next few days the output of urine increased. By October 24, however, the blood urea had dropped to 34 gm. for each 100 c.c. Edema was first noted on this day; it was only moderate, being especially noticeable around the lumbosacral region, and in the hands and feet. Fluids were then restricted to 1,500 and 1,800 c.c. and the administration of caffeine was begun. Gradually the output of urine increased and coincident with this the edema disappeared so that two weeks after the operation the patient was entirely free from edema, and the blood urea was 33 mg. for each 100 c.c. Urinalysis disclosed albumin, graded 1, and an occasional pus cell. During this period of acute renal insufficiency the blood pressure was taken several times, and the highest reading recorded was 120 systolic and 70 diastolic. The serum protein values, and the blood fat and blood cholesterol values were normal. Toxemia was marked; there was some drainage from the wound; slight fever, frequent hiccup, and vomiting occurred. The patient was dismissed from the hospital thirty-four days after the operation at which time he was voiding a normal quantity of urine. The blood pressure was still normal. The blood urea was 28 mg. for each 100 c.c. The urine contained albumin, graded 1, and an occasional pus cell. Cardiac conditions were the same as on admission; at no time had there been an appreciable degree of cardiac decompensation. The two short attacks of auricular fibrillation were the direct result of the intravenous injections.

Case 3.—A man aged sixty-seven came to the Clinic because of progressive constipation, slight bleeding from the rectum, and a lump in the left lower quadrant of the abdomen.

The patient had lost 28 pounds in weight during the last year, but otherwise appeared in fairly good health. The hemoglobin (Dare) was 80 per cent, and erythrocytes numbered 4,700,000. The Wassermann test was negative. Blood pressure was 130 and 80. Moderate arteriosclerosis was noted in the radial and retinal arteries. The heart did not appear enlarged and the sounds were not abnormal. The prostate was slightly hypertrophied. There were no symptoms of cardiorenal-vascular disease except occasional nocturia. Urinalysis was negative for albumin, casts, blood, and pus. The specific gravity of the urine was 1.026. Tests of blood urea and phenol-sulphonaphthalein return were not carried out. A diagnosis of carcinoma of the descending colon and sigmoid was made and operation advised.

October 31, 1927 colostomy was performed, and the patient recovered

uneventfully. One week after operation the specific gravity of the urine was 1.022; it did not contain albumin, casts, blood, or pus. Two weeks after the first operation the carcinoma was removed by anterior resection. The operative wound became infected and began to drain shortly after the operation, but the patient seemed to be doing fairly well for five days, even though the output of urine was not quite satisfactory. Oliguria became more marked on the fifth day after operation, and the patient was drowsy and nauseated. The blood urea was 148 mg. for each 100 c.c. of blood, and the carbon dioxid combining power of the plasma was 40 per cent by volume. The phenolsulphonephthalein return was only 15 per cent in six hours, due chiefly to the marked oliguria. Only 85 c.c. of urine was obtained from the bladder by catheter during the six-hour period. Urinalysis revealed a trace of albumin, and an occasional red blood cell. The blood pressure was 130 and 70. There was no edema. From 3,000 to 4,000 c.c. of fluid was given daily; part of this was given intravenously in the form of 10 per cent glucose. Caffein sodium benzoate was given subcutaneously. Under this regimen the fluid output increased somewhat and the blood urea dropped to 72 mg. for each 100 c.c., but the patient showed signs of peritonitis, became more and more toxic, and died ten days after the second operation. A diagnosis was made of low grade peritonitis and acute toxic renal insufficiency.

Necropsy data were as follows: (1) recent (twenty-three days) colostomy opening and infected wound from resection of carcinoma at the juncture of the sigmoid and descending colon; (2) separation at anastomosis, and local subperitoneal abscess and general peritonitis; (3) ileus (graded 3) and dilatation of stomach (graded 3); (4) metastasis to the left iliac lymph nodes; (5) edema of the lungs; (6) acute ulcerations of stomach and duodenum; (7) healed tuberculosis of lungs; (8) arteriosclerosis (graded 3); (9) hyaline perisplenitis; (10) cholesterosis (graded 2) and (11) cyst of left kidney.

The pericardium was 10 cm. in transverse diameter and when opened contained 5 c.c. of clear fluid. There were no clots in the pulmonary artery. The heart weighed 325 gm. The epicardium was smooth and glistening. The muscle was pale brown and faintly streaked. The cardiac chambers and the endocardium were normal. The coronary arteries showed sclerosis (graded 1+). The measurements of the heart valves were normal. The right kidney weighed 121 gm. The capsule stripped with ease, leaving a slightly granular surface which contained several cortical cysts measuring from 3 to 5 mm. in diameter. Fetal lobulations (graded less than 1) were present. The stellate veins were distinct. On cut section the cortex measured 6 mm. and the medulla 1.5 cm. The corticomedullary markings were quite distinct. The pelvis was normal and there was no increase in peripelvic fat. The left kidney weighed 132 gm. The capsule stripped with ease, leaving a granular surface in which the veins were quite prominent and fetal lobulations were present (graded less than 1). A cortical adenoma 1 mm. in diameter, white and circumscribed, was present. A cortical cyst measuring 3 mm. in diameter was situated in the upper pole and extended directly into the pelvis. The organ was rather firm in consistence. The cortex measured 6 mm. and the medulla 1.8 cm. The cut section appeared similar to that from the right kidney. Microscopically there were no changes sufficient to account for the

acute renal insufficiency; the kidneys appeared normal for a man aged sixty-seven. The glomerular tufts appeared normal and filled the capsular spaces. There were no collections of cells in the tufts or in the spaces. The convoluted tubules were regular in shape and size and the tubular epithelium was not compressed. The nuclei of the tubular epithelial cells were distinct and uniformly stained. There were no hyaline deposits in the tubules, and no appreciable increase in interstitial connective tissue. Nowhere in the section was there evidence of exudative or inflammatory phenomena (Fig. 272).

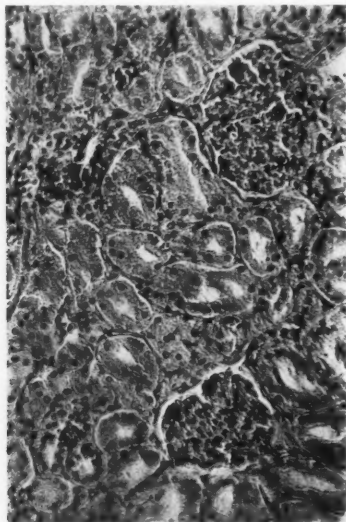


Fig. 272.—(Case 3.) Section from kidney showing almost normal appearance ($\times 100$).

Case 4.—A woman aged sixty-one came to the Clinic November 1, 1927 because of a rectal tumor. Nine months before admission persistent bloody diarrhea had developed, and this had changed to progressive constipation with gas and cramps in the lower part of the abdomen. Two and a half months before admission a tumor was found in the rectum. The patient had lost considerable weight and seemed somewhat weak.

On examination carcinoma of the rectum was found. The hemoglobin (Dare) was 66 per cent; erythrocytes numbered 4,690,000 and leukocytes 6,800. The blood pressure was 130 and 65. There was slight arteriosclerosis. The heart did not appear enlarged, and sounds were not abnormal. There were no symptoms of cardiorenal-vascular disease except a little difficulty in voiding urine, noted only after frequent rectal examinations. The specific

gravity of the urine was 1.024; there was no albumin, sugar, casts, or red blood cells, and only an occasional pus cell. Estimations of the blood urea and the phenolsulphonephthalein excretion were not made.

Colostomy was performed November 10. The patient's recovery was uneventful. Twelve days after the first operation the growth was removed anteriorly. The pathologist reported colloid adenocarcinoma with lymphatic involvement. The patient did not do well immediately after the second operation. Oliguria was marked and the blood urea rose to 89 mg. for each 100 c.c. The specific gravity of the urine was 1.019; albumin graded 2, an occasional hyaline cast, many granular casts, and an occasional pus cell were present. Blood pressure was 120 and 65. Fluids were forced up to 3,000 c.c. daily, 1 liter daily of this being given intravenously in a 10 per cent solution of glucose. Caffein sodium benzoate, and digifolin were given hypodermically with slight increase in the output of urine, but abdominal tenderness, distention, and signs of peritonitis had developed. The patient failed rapidly, and died on the fourth day after the second operation. A diagnosis was made of peritonitis following resection of carcinoma of the rectum, and acute toxic renal insufficiency.

Observations at necropsy were as follows: (1) recent (fourteen days) colostomy opening, and generalized peritonitis from anterior resection of carcinoma of rectum; (2) cholecystitis with ulceration of juncture of gall-bladder and cystic duct and cholelithiasis (three stones) with diverticulum at fundus; (3) metastasis to sacral and iliac lymph nodes; (4) healed tuberculosis of spleen, lungs, and hilum nodes; (5) arteriosclerosis, (graded 3); (6) arteriosclerotic changes of kidneys (graded 2); (7) fatty changes of liver (graded 2); (8) complete duplication of right kidney, pelvis, and right ureter with strictures of the uterus to the upper major calix, and (9) leiomyoma of uterus. The transverse diameter of the heart was 9 cm., the weight was 279 gm., and its consistence was firm. The epicardium was smooth and glistening throughout. The endocardium was apparently normal. The pericardial fat was graded 2. The valves appeared normal and the measurements were normal. Coronary sclerosis was graded 1. No streaking of the muscle was seen on tangential section. The left kidney weighed 172 gm.; the capsule stripped with ease leaving a smooth, pink, slightly granular surface. Fetal lobulations (graded 1) were present. On cut section the markings were quite distinct. The cortex measured 3 to 5 mm., and the medulla 1.4 to 1.6 cm. The pelvis was apparently normal. The right kidney weighed 205 gm. The capsule stripped with ease. The cut section appeared as in the left kidney.

Two distinct pelves, one near the upper pole and one near the lower, and two distinct ureters to the bladder on the right side were present. The ureters were both somewhat constricted 8 cm. from the juncture at the bladder. The bladder appeared normal.

Microscopic examination of the kidneys disclosed few abnormalities. The glomerular tufts appeared normal and filled the capsular space. There were a few hyaline fibrosed glomeruli near the outer margin of the cortex. The convoluted tubules were regular in shape and size, and the tubular epithelial cells were distinct and uniformly stained. There were no hyaline deposits

	Temperature.	Blood pressure.		Blood.						Urine.					Comment.	
		Systolic.	Diastolic.	Hemoglobin, per cent.	Urea, mg. per cent (Dare).	Creatinin, mg. per cent.	Carbon dioxide combining power, per cent by volume.	Twenty-four-hour fluid intake, c.c., besides fluid in stool	Twenty-four-hour specimen, c.c.	Specific gravity.	Albumin, grade.	Casts.	Red blood cells.	Pus cells.		
Case 1, man aged fifty-one																
Before operation.....	99	100	68	71				2000	975	1.006	0	0	0	0	Patient comatose; slight edema. Edema, graded 1 to 2. Abscess left thigh drained. Slight cystitis following catheterization; no edema. General condition fairly good. No recurrence of carcinoma. No cardiovascular symptoms.	
Second day after operation.....	101				22		57	3610	550							
Eighth day after operation.....	102				34		45	3000	1225							
Tenth day after operation.....	100	130	80	70	120		55	2900	1950	1.012	1	0	1	1		
Twelfth day after operation.....	100.5				200		53	2700	1925							
Thirteenth day after operation.....	100				70		54	2350		1.010	1	0	occ.	0		
Fifteenth day after operation.....	101	118	65	70	22	1.2	54	3300	3445	1.010	2	0	0	2		
Twentieth day after operation.....	101	124	70		26	1.9		2030	2790		tr.	0	0	1		
Thirtieth day after operation.....	101							3650	3050	1.007	1	0	0	occ.		
Sixty-third day after operation.....	98.6	120	75	52	30					1.015						
Eleven months after operation.....	99															
Case 2, man aged sixty-four																
Before operation.....	98	130	80	70				2950	900	1.020	0	0	0	0	Auricular fibrillation following intravenous injection. Extreme toxemia; frequent hicough. Edema 1+. Edema disappearing; patient much improved. No edema. Still some infection of wound. No edema.	
Third day after operation.....	101							2625	310	1.025	1	1	0	occ.		
Fifth day after operation.....	100	120	74		70			2650	800	1.023	2	0	0	occ.		
Sixth day after operation.....	99.5				80											
Eighth day after operation.....	100				34			2400	825	1.019	1	0	0	occ.		
Tenth day after operation.....	100	120	72		25			1015	1015	1.010	1	0	0	1		
Fifteenth day after operation.....	100.5				33			1890	1420	1.012	1	occ.	0	1		
Thirty-fourth day after operation.....	99	118	65		28			2350	1550+	1.009	1	0	0	occ.		

in the tubules. In some places the tubular epithelium seemed detached from its basement membrane, but this was thought to be an artefact. There was a slight localized increase of interstitial fibrous tissue around some of the interlobular arteries. Some of the larger arteries showed slight mesial thickening. Nowhere in the section was there evidence of true exudative or inflammatory phenomena. The few changes present were typical of a slight arteriosclerotic atrophy (Fig. 273).

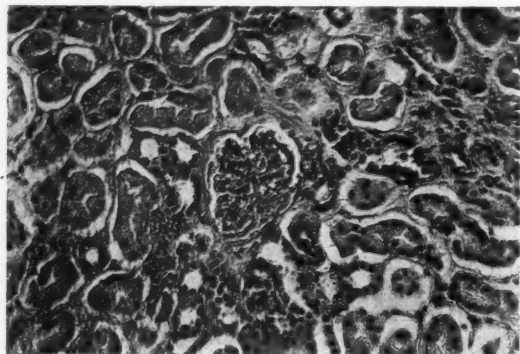


Fig. 273.—(Case 4.) Section from kidney showing only a few arteriosclerotic changes ($\times 100$).

Oliguria and elevated blood urea were the chief and most constant signs of renal insufficiency. Edema, if it occurred, occurred later. Blood pressure was normal, and the abnormal conditions in the urine were inconstant (Tabulation, pages 1578 and 1579).

COMMENT

A toxic state was present in all of these cases. In most of them there had been partial obstruction of the bowels for some time before operation, and some infection always occurred in the operative field. These factors, when added to a certain amount of cachexia in elderly patients, would seem to explain the development of the renal insufficiency. Lesions of the kidney were variable. In none of these cases was there typical evidence of acute glomerulonephritis. The clinical course is similar to that in cases of diffuse degenerative renal lesions, and although such lesions probably occur it has been surprising to find in several cases almost normal appearing renal structures (Figs.

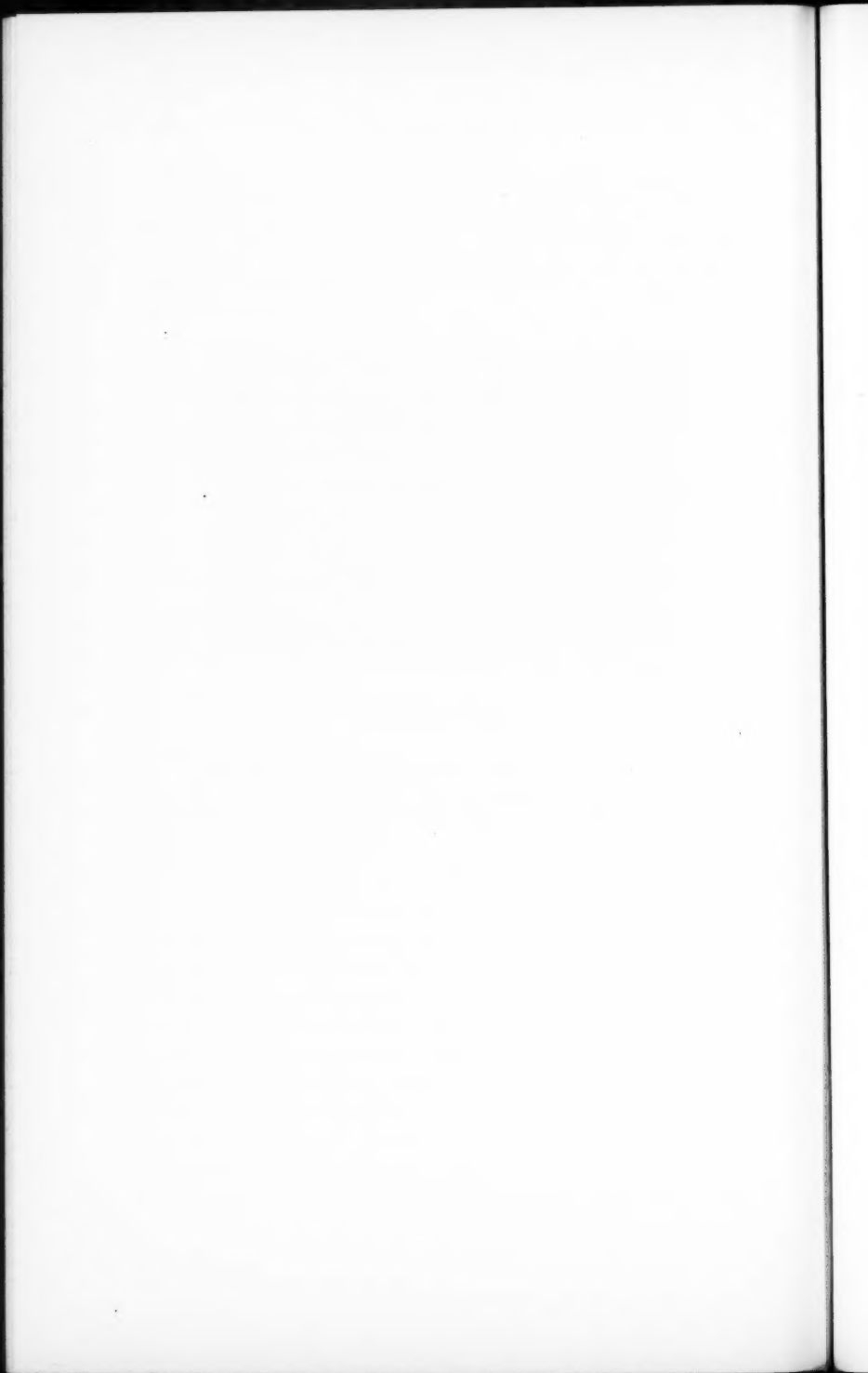
272, 273). The slight changes found may be no more than would occur in a similar group of elderly patients without renal insufficiency. Further study is being carried out in an attempt to determine this point. Renal insufficiency of this type occurs quite frequently in association with different toxemias.^{1,2} We have selected this special group of cases for study because it would seem that the occurrence of renal insufficiency has not been sufficiently emphasized. The use of a liberal fluid intake (2500-3000 c.c. daily) and diuretics of the caffeine type have brought about satisfactory diuresis in many cases. Frequently the best results have been obtained if some of the fluid is given intravenously in the form of hypertonic glucose solution.

SUMMARY

Acute renal insufficiency often occurs following operations for the removal of carcinoma of the lower part of the colon and the rectum. Early recognition of this condition and the institution of proper treatment frequently results in prompt recovery.

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RECURRENT ATTACKS OF UNCONSCIOUSNESS

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THERE are probably few of us who have not suffered at some time in our lives transient loss of consciousness from injury, illness, or emotional stress. In each case, while the experience has been a disagreeable one, it usually descends into the limbo of the forgotten without creating alarm in our minds. However, the situation is quite different if repeated attacks of loss of consciousness occur without apparent cause and without signs of abating, even though health seems to be normal between attacks. The sufferer experiences a distinct feeling of anxiety and dread of future attacks. It is not pleasant to be stricken unexpectedly and mysteriously at the most inconvenient time and in the least desirable of places, not to mention being a subject of morbid interest to the casual onlookers.

The type of patient under discussion is represented by those who present themselves for examination without obvious physical signs of cardiac, renal, or cerebral disease, and yet lose consciousness periodically. Too often all that is available is the personal description of the patient, necessarily limited as to the phenomena occurring during the attack, or the story of an attendant relative or friend who is usually too excited during the episode to give coherent details. In any event the patient demands to know the nature of the attack and the possibilities for the future. Occasionally the examiner is privileged to witness one of the attacks, and this experience is worth infinitely more than all the descriptions given by the patient or onlookers. An unexpected attack in the office may result in a revisal of judgment both as to the nature of the disease and the ultimate prognosis. Before a final opinion is passed, therefore, it is always best to wait until the patient has been seen in an attack and all details verified.

A relatively common type of recurrent attacks of loss of consciousness occurs in rapidly growing, usually tall, lanky adoles-

cent persons, somewhat frail physically, and often presenting obvious signs of vasomotor instability.

REPORT OF CASES

Case 1.—A girl aged eighteen came to the Clinic October 14, 1925 complaining of "fainting spells." For three years lapses of consciousness had occurred at irregular intervals: about fifty or more in the first year, twenty in the second, and two or three in the third. The attacks came on suddenly while the patient was standing and she would cry out, "I am going to faint." She felt herself gliding into unconsciousness, surrounding objects faded away, sounds became gradually more distant and she dropped to the ground, lying limp and pale, and breathing imperceptibly, the pulse rapid and feeble. After from three to five minutes color, pulse, and respirations returned to normal, and she gradually became conscious without any mental confusion, and was able to assume normal activities almost immediately. Predisposing causes for attacks are usually emotional upsets, such as a quarrel with relatives, pain from accidental injuries, fatigue, or the sight of blood.

The patient was tall and poorly developed. Her extremities were cold; she blushed readily and exhibited marked dermatographia. A diagnosis was made of syncopal attacks due to poorly balanced circulatory apparatus.

It is difficult to distinguish such symptoms from the more serious manifestations of epilepsy, but there are certain features about the attacks that make it easy to recognize their true significance. There are always predisposing factors bringing on the attack, namely pain, hunger, standing too long, poor ventilation of rooms and emotional disturbances. The patient's relatives may volunteer the statement that he or she has always "fainted" easily, and the general physical appearance helps in assessing the seriousness of the condition. The attacks themselves are presumably due to transient cerebral anemia secondary to faulty circulatory balance. With increasing age and rounding out in physical configuration, the attacks generally become fewer and fewer and finally disappear. The essential feature in the type of loss of consciousness is the relatively slow onset. Consciousness is not abruptly lost, but usually fades out with the associated phenomena of dimming of vision, recession of sounds, pallor, and muscular relaxation. The type of disturbance illustrated in Case 2 is very different.

Case 2.—A man aged twenty-one came to the Clinic May 14, 1927 because of "fainting attacks." Twelve months previously, while undergoing

military drill at school, he suddenly experienced a peculiar "light-headed, dizzy" sensation and immediately lost consciousness. Onlookers at the time said that he looked blank, stared straight ahead, and walked slowly backward out of the ranks in which he had been drilling. He made some utterly irrelevant remark while moving away, then walked aimlessly across the courtyard and sat down on a bench. After one or two minutes his face resumed normal expression and he regained consciousness. For about five to ten minutes he was somewhat confused mentally, then returned to normal, but expressed a desire to sleep and was put to bed where he slept for several hours. Following the initial attack the attacks varied from five in a day to one in two weeks. Each attack was similar to the first; they varied little in essential features. The attacks came at any time or place, and on each occasion were represented by sudden complete loss of consciousness and slow recovery with mental confusion and drowsiness. The patient himself sometimes had no recollection of attacks when they came frequently; they always came on spontaneously without associated circumstances that the patient or his family could recognize. The attacks might appear during a meal, while the patient was sitting quietly reading a book, or in the midst of conversation. Usually after about fifteen minutes he could resume the occupation that had been interrupted. Some of the attacks were slight, and were recognized by the relatives only by his peculiar blank expression and the sudden cessation of whatever activity he might be engaged in.

The patient was well developed and intelligent. In all the routine of physical examination nothing obvious was found to explain the attacks. A diagnosis of petit mal was made, and a very uncertain prognosis given.

The outstanding characteristics of the disease were the sudden attacks of transient, yet complete loss of consciousness recurring again and again without apparent cause. The attacks were short, yet stereotyped, and the patient had normal health in the intervals. With all their brevity and relatively infrequent occurrence the patient had no difficulty in recognizing them each time they appeared in their suddenness and the completeness with which they influenced consciousness. The patient's relatives were also quick to recognize the reappearance of the attacks in the strange facial expression and automatic behavior of the sufferer. Petit mal attacks vary in severity and degree from patient to patient, yet all are essentially alike in spontaneity of appearance, short duration, and persistent recurrence in the same form for the individual patient. They may persist without associated phenomena throughout the patient's life, the patient enjoying normal health without mental deterioration between attacks. Usually, after a certain

period of petit mal attacks, the more violent and disagreeable phenomena of grand mal develop. Later the two appear together with many more of the petit mal than grand mal attacks. Frequently a series of minor attacks precedes a general convulsion.

Case 3.—A girl aged eighteen came to the Clinic October 19, 1927 because of recurrent convulsive seizures. Three years previously while dressing in the morning she suddenly and without warning fell to the floor unconscious. All the muscles were rigid and the face became deeply cyanosed. In a few seconds quick jerking movements of the muscles of the face, jaws, and extremities ensued and she bit her tongue, breathed heavily, and bloody foam exuded from her mouth. She expelled urine involuntarily. After a few minutes these jerking movements died away to be followed by relaxation and stupor. Later she passed into a sound sleep which lasted about two hours. On awakening she felt tired, sore in all muscles, had a severe headache, and a swollen and lacerated tongue. The next day she was apparently normal, but within a few weeks the same phenomenon was repeated and it kept recurring. In the first year she had nine attacks, in the second six, and thereafter three or four a year until the current year when they appeared every month or even more frequently. Besides the major attacks described, minor attacks, consisting simply of transient loss of consciousness, also occurred.

The patient was well developed, intelligent, and without any stigma of degeneration. The complete physical examination was essentially negative. A diagnosis of grand mal and petit mal was made.

This patient was therefore considered to be afflicted by a disease, knowledge of which goes back into the mists of antiquity. Unfortunately our knowledge only covers the phenomena that can be observed, the deeper significance of the disease, its cause and cure all being relatively unknown. It is an unsatisfactory disease for the modern physician to treat. He can give no assurance as to the future, can only apply palliative measures, and can give no adequate explanation for its appearance.

It is not within the scope of the present discussion to cover all of the different types of grand mal with their individual problems of etiology, prognosis, and treatment, but to emphasize the recognition of the disease and its distinction from other convulsive manifestations, notably hysteria. As in petit mal there is a stereotyped sameness of attacks in the individual patient. The attacks may differ in degree but not in kind. The characteristic features are, first, the sudden and complete loss of consciousness with or without an aura. As in petit mal

the attacks are relatively short except in cases of status epilepticus. A grand mal attack is seldom protracted longer than twenty to thirty minutes from its onset. Again there is the spontaneity of appearance at any time or place: in public or alone, at midnight or at noon. There is, therefore, the same tragic sense of insecurity. Consciousness is lost completely, and any movements that occur during the attack are automatic, purposeless, and without emotional significance. The manner in which the patient describes his trouble is significant. He describes it simply, without elaboration and with little display of emotion; he is even cool and meticulous as to the number, frequency, and severity of attacks. Often he keeps a diary. Usually, however, he dislikes to discuss his trouble, he has little interest in it except to get rid of it, and the whole story of events is soon over. A sufferer from grand mal is never humorous concerning his trouble. To him it is a deadly affliction. A contrasting situation is shown in Case 4.

Case 4.—A girl aged eighteen was brought to the Clinic October 31, 1927 because of convulsive attacks. Five months previously she had been in training as a nurse but became so restless, nervous, and irritable that she had to stop work and return home. Soon afterward she began to have attacks of unconsciousness. The first attack occurred while she was washing a large pile of dishes, following an evening of festivity at which she had become greatly fatigued. She felt weak and nauseated, objects became dim, and she sank limply to the floor. Her color remained normal and she revived promptly with a dash of cold water on the face. Thereafter many attacks occurred, usually when the patient was tired or emotionally disturbed, and particularly when she was engaged in some arduous monotonous task. During this period she became infatuated with a young man of whom her parents disapproved and she became secretly engaged to him. Parental pressure was applied to separate the two and then her simple falling attacks became more complicated and prolonged. As before, she sank gradually into unconsciousness, but during attempts of parents or friends to arouse her considerable motor activity developed. She tore her hair out in handfuls, scratched her breast with her nails until deep furrows appeared, ground her teeth, and snapped viciously at those around her, once just missing her mother's hand. She chewed her tongue until it bled, but instead of clonic jerking of the jaws the chewing was well coordinated and volitional. Her arms and legs moved continuously in well directed kicks and blows. Once she knocked her father half across the room with a resounding slap in the face. She threw pillows off her bed and hurled her shoes at her relatives, all the time moaning, groaning, weeping, and carrying on a highly emotional performance. After one or two hours of

this, when she and the family had become thoroughly tired, she gradually regained consciousness, manifesting complete ignorance of what had occurred. These attacks were repeated once or twice a week, or oftener, and her family were at their wit's end.

The patient was large, overnourished, muscular, somewhat retarded mentally, but seemingly in excellent physical health so far as revealed by ordinary examination. Her general behavior during the taking of the history was significant. She was childish, silly, and talkative. She seemed to regard her illness as a joke, was immensely interested in the description of her attacks as given by her mother, and exulted in some of the more lurid details. She insisted that she was completely unconscious while the attack was on. Her emotional reactions changed, however, when an attempt was made to adjust the family conflict relative to her proposed nuptials, and joviality was replaced first by chagrin and later by temper. The diagnosis was constitutional psychopathic inferiority and hysterical convulsions.

The characteristics in this case were the complicated nature of the attacks and their long-drawn-out course, the marked emotional dramatic and excitable atmosphere, and the fact that an audience was seldom lacking during attacks. All the motor activity was well coördinated, purposive and directed toward an end, for example, snapping at her mother's fingers with her teeth. The variability of the attacks was characteristic also. Seldom does an hysteric person repeat the performance, and the stereotyped manifestation of epilepsy is lacking. Finally there was the patient's reaction to her trouble with the barely concealed pride in the performance, and the facetious spirit in which it was regarded. The prognosis in these cases is not good. There is, of course, a tendency for the attacks to cease under proper adjustment of environment, but the patient still possesses a poorly endowed, unstable personality which can be expected to break out in other ways. It is difficult to treat such patients.

A milder form of hysterical lapses of consciousness is represented by those patients who are intolerable to moderately severe pain, and in whom a protective amnesia develops for the unendurable part of it. This is not of great significance when an attack of pain is but one episode in the patient's life. In cases of frequently recurring migraine headaches, these lapses of consciousness become of significance diagnostically.

Case 5.—A man aged thirty-one came to the Clinic April 21, 1923 complaining of severe headaches and attacks of unconsciousness. At the age of sixteen severe migraine headaches had developed, with a definite sequence of symptoms. A day before an attack he usually felt unusually well. On the morning of an attack he felt drowsy, lethargic, and "bilious." The attack began suddenly with dimness of vision which increased to complete blindness in thirty minutes. This cleared up rapidly to be replaced by severe throbbing unilateral temporal headache, which increased in severity to become almost unbearable in an hour or two. He usually went to bed at the onset of the visual disturbance, and when the headache reached its height he became unconscious. All muscles were rigid, teeth were clenched, hands tightly closed, and he groaned and moaned continuously. This might last for several hours but for the administration of a narcotic hypodermically. Usually the patient had no recollection of this, but following its administration he relaxed, went to sleep, and awoke a few hours later tired out and weak, but free from headache. Without the narcotic the phase of unconsciousness, rigidity, and groaning lasted longer, ending after two or three hours in relaxation and sleep. During the unconscious period the patient could not be roused, and did not respond except by resisting all handling and examination. These attacks had occurred about once a month for fifteen years. The patient had not had headache between attacks and had not been unconscious. A diagnosis was made of migraine with hysterical amnesia.

Actually the lapse of consciousness in this case was hysterical, yet protective in that at the height of the pain of a severe migraine headache all sensation was abolished. The same phenomenon may occur in unduly sensitive persons during gallstone attacks, the colic from a renal calculus or following a painful injury.

The patients described in the foregoing cases have been relatively young. Toward the close of life certain manifestations characterized by simple lapses of consciousness or convulsive seizures may appear as is shown in Case 6.

Case 6.—A banker aged sixty-four came to the Clinic May 21, 1926 because of attacks of mental confusion. The first attack had occurred a year previous to admission while he was speaking at a Chamber of Commerce dinner. He became confused rather suddenly, and had to stop speaking for about half a minute. He was then able to take up the thread of his discourse, and finished his talk with some embarrassment. During the following year he had five or six such attacks. His wife noticed that during attacks he suddenly became pale, his face assumed a peculiar expression, and he talked disconnectedly and at random and then in a few minutes just as suddenly returned to normal. The attacks came in a series of two or three within an

hour and then there were no more for about two months. On one occasion while driving a car in traffic he smashed into the rear end of the car in front. He did not realize that he had done so until he recovered. Attacks were more likely to come on under heavy stress and strain of business. The patient was not sure that he lost consciousness during attacks but his wife thought he did. He had noticed about the time of onset of the attacks that his memory failed, that he became increasingly irritable with his employees, and that his business judgment was not as sound as it had been. Emotional control was also becoming poor with a tendency to cry over sad events in picture and in story.

The patient appeared to be healthy and was somewhat overweight. The systolic blood pressure was 168 and the diastolic 82. There was moderate sclerosis of peripheral arteries, but no obvious lesions of the heart. Ophthalmologic examination showed mild sclerosis of the retinal arteries and marked reduction in caliber. A complete neurologic examination gave negative results. A diagnosis of cerebral arteriosclerosis was made.

The patient was seen again October 1, 1927, when he returned for re-examination. The attacks of mental confusion and unconsciousness had persisted for six or seven months in the intervening period of eighteen months. There had been no other change except that he was gradually retiring from active business.

It is surprising how frequently such a condition as that described in this case occurs if patients have led a strenuous, energetic, intellectual life. It seems to be relatively more common in those who have had to use their brains rather than their muscles to gain a livelihood. The attacks may be considered to be the initial sign of that decay which is the fate of all eventually. Nevertheless, they may be present for many years with little or no other signs before final dissolution begins. Physical signs of disease in such cases may be slight, and the only indication of cerebral arterial disease is in the sclerosis of the retinal arteries, as seen in ophthalmologic examination. Deafness, failure of memory, and mental deterioration are, however, frequent concomitants.

Cardiac disease was not found in any of the foregoing cases. It is usually first thought of by the public in cases of recurrent attacks of unconsciousness. Rightly it should be the physician's duty to exclude cardiac disease as a cause, and yet there are few diseases of the heart that can produce recurrent attacks of unconsciousness over a long period of time without something more serious happening. Heart-block or Stokes-Adams syndrome is rare and can be readily recognized clinically, but a more com-

mon disease and one easily forgotten is the condition known as paroxysmal tachycardia. Barnes* gave the first clear, complete and comprehensive account of the cerebral manifestations of paroxysmal tachycardia. Vertigo, syncope, and even epileptiform convulsions may occur during an attack and the condition may remain unrecognized, because the patient's complaint of cardiac symptoms was not given the proper attention and no signs of cardiac disease were found between attacks. If the condition is suspected and an opportunity given to witness an attack, the diagnosis is easily made. Without this suspicion the patient's attacks of unconsciousness may be classified wrongly as epilepsy.

Convulsions, lapses of consciousness, syncopal attacks and the like are all necessarily symptomatic of a causal disease known or unknown. A diagnosis of idiopathic or essential epilepsy represents primarily a confession of ignorance and worse, it tends to lead to a smug self-satisfied assumption of the full significance of the attack and the course of the disease in the future. This may ultimately be wholly unjustified, especially in recent cases of convulsive attacks when no cause is found. An open verdict should be given until future events give some clue as to the nature of the process. It may take months or years before this is brought about, but it is seldom possible in a given case of epileptiform seizures of a few months' duration to exclude serious cerebral mischief that may later demonstrate its presence.

Case 7.—A woman aged fifty-six came to the Clinic June 7, 1922 complaining of convulsive attacks. The first convulsion, epileptiform in character, had occurred two years before. Convulsions recurred every three months and were moderately severe, but without symptoms between attacks except slight failure in memory. There had been no headaches.

The patient did not remain for complete examination and a diagnosis could not, therefore, be made. She was seen again two and a half years later. This time she was brought to the Clinic in an ambulance and was in deep stupor. In the interval attacks had become more frequent and more severe, and were preceded by transitory unpleasant tastes and odors. A year previously the attacks had ceased suddenly and did not occur for eight months,

*Barnes, A. R.: Cerebral manifestations of paroxysmal tachycardia. *Am. Jour. Med. Sc.*, 1926, clxxi, 489-495.

but mentally she became dull, forgetful, and apathetic. Two months before the second visit all symptoms returned and were more severe. Headache, nausea, and vomiting came between convulsions and, following a more severe convulsion a few days before, complete left hemiplegia, progressive stupor, and involuntary urination developed. Examination was limited because of the stupor, but complete flaccid paralysis of the left side of the body was noted. Eye-grounds were normal and the spinal fluid was not under great pressure. Because of the history of convulsions with olfactory and gustatory aura, the left hemiplegia and progressive downward course, a diagnosis was made of tumor in the right temporal lobe. The patient died four weeks later and necropsy proved this diagnosis to be correct.

The point of emphasis in this case was that for at least three years all that the patient suffered from, according to the history, was the epileptiform attacks. Their true significance could easily have been overlooked during that time and the case be passed as one of epilepsy. It was only in the last few months of life that a diagnosis of brain tumor could have been made with any certainty, and it was then too late to accomplish anything for the patient. In every case of recent epileptiform attacks, unless there is some obvious cause, tumor should be suspected and the patient kept under observation until time confirms or rules out this suspicion.

In this series of cases, such as are frequently seen in office practice, an attempt has been made to demonstrate some of the attending problems and their possible solution. The diagnosis is always difficult from the patient's and the relatives' story of events. It is far better to await the opportunity to observe an attack in all its manifestations. A physician should not be in too great hurry to offer an opinion, since such an opinion will be accepted as binding by the patient both for his present predicament and for all events in the future. It is far better to wait and obtain all the facts possible in the case and try to rationalize on these, rather than be satisfied with some unscientific worn-out term that means nothing.

OSTEITIS INVOLVING THE BONES OF THE PELVIS

CHARLES G. SUTHERLAND

A REVIEW of the voluminous literature on osteitis shows that although many forms of the disease have been discussed clinically and roentgenologically, they have often been classified pathologically in a single group, or at least as modifications of a single pathologic process.

Dawson and Struthers in 1923 presented a complete review of the subject of generalized osteitis fibrosa, and discussed the various types. They described the chronic inflammation of bone reported by Paget in 1877, also the lesion described by von Recklinghausen in 1891, crediting von Recklinghausen with first considering osteitis fibrosa as essentially inflammatory in origin and later modifying his view to include it in the group of metaplastic malacias, thereby bringing it into relation with anomalies of metabolism. They then compared osteomalacia and rickets, the two most important malacic conditions, with osteitis deformans and osteitis fibrosa. •McFarland has discussed osteitis deformans, osteomyelitis fibrosa, osteitis fibrosa cystica, osteitis hemorrhagica, benign bone cysts, and benign giant-cell sarcoma; he considers them "pathologically so inextricably linked together as to appear to be but variations of the same morbid process." Wilhelm in 1925 presented a comparative anatomic and roentgenologic study of osteitis fibrosa and the hyperostotic form of bone syphilis.

Roentgenologically most of the foregoing diseases have definite characteristics by which they may be distinguished, and not all of them are concerned in a discussion of lesions involving the pelvic bones. In fact, a study of films depicting pelvic lesions which are somewhat similar roentgenographically, brings into consideration osteitis deformans (Paget's disease), osteitis

fibrosa of undetermined origin, osteoplastic and osteoclastic metastasis, multiple myelomas, and the hyperostotic form of bone syphilis. Four of these deal with bone destruction and bone proliferation which results in increased radiopacity of the bone, in the other two with increased radiotranslucency. Practically, the discussion becomes narrowed to the differentiation of the roentgenographic characteristics of osteitis deformans and



Fig. 274.—Osteitis deformans (Paget's disease). A coarsely mottled shadow with multiple striæ throughout, and thickening of the cortex of the femurs were noted. In the left ilium are multiple cysts in which giant cells were found.

the osteoplastic form of metastasis; on the proper interpretation of these shadows depends the prognosis of the life expectancy of certain persons. Failure to interpret them may result in great injustice to the interests of the patient, whichever way the opinion may err. A complicating factor is that both diseases are common at the same age period, that is, from the fifth decade on, and that in this period changes in bone due to arthritis and senility are also most common.

One of the great advantages attributed to roentgenology has been the opportunity to study pathologic changes in the living; it may be pertinent, therefore, to consider the pathologic changes and compare them with the roentgenographic data. The histologic changes in bone in osteitis deformans are: (1) extensive resorption of bone by osteoclasts; (2) excessive formation of new bone, laid down by osteoblasts on the surface of the old resorbed bone, so that the cortex which had become rarefied becomes



Fig. 275.—Osteitis fibrosa of undetermined cause. The roentgenologic characteristics suggest osteitis deformans. There is no involvement of the femurs. Roentgenograms of head were negative.

dense, especially in the skull; (3) transformation of bone into fibrous tissue, with encroachment on the cortex, and the laying down of osteoid bone in this fibrous tissue, the lamellæ of which run in every direction; (4) the formation of subperiosteal layers which add to the volume of the bone, and (5) the occasional occurrence of cysts or spaces filled with fluid in the fibrous tissue, or of tumor-like masses with numerous giant cells. The roentgenogram of osteitis deformans (Fig. 274) at least suggests

the added thickness of the bone; the bones of the pelvis look larger, and when the femurs are involved the pathognomonic sign of osteitis deformans, the marked thickening of the cortex, appears. In the shadow the bone appears coarsely mottled, with multiple striæ running throughout; rarely is the formation of small or large cysts apparent. In doubtful cases roentgenograms of the skull and tibia may reveal the characteristic thickening of the cortical layers. I have observed cases which clinically and roentgenologically were osteitis deformans (Fig. 275), in which the femur, the head of the femur, and the tibia failed to show involvement.

Carcinomatous osteitis is the name given by von Recklinghausen to the pathologic processes seen in cases of carcinoma of the prostate. Ewing says that marked osteoplastic skeletal metastasis occurs in a notable group of cases of prostatic carcinoma. Similar osteoplastic processes, he says, are observed with mammary carcinoma, and with tumors of the stomach, gallbladder, thyroid, and so forth, but early and frequent occurrence and extensive distribution belong chiefly to prostatic carcinoma. Ewing summarizes the pathologic characteristics as the lodging of tumor cells in the small venous sinuses, causing stasis and hemorrhage, which is followed by a reactive growth of fibrillated, osteoid, and finally osseous tissue. The tumor cells become enclosed in the bone, assuming the function of osteoblasts, and bony tissue may become most abundant in cellular areas of the tumor where connective tissue is lacking. Participation of connective-tissue osteoblasts is also observed. Extensive resorption of new bone by osteoclasts may follow the plastic process. There is little actual new growth but chiefly absorption and redeposit of the old. Cyanotic hyperemia, inflammatory changes in the marrow, and primary necrosis of bone are considered of secondary importance. Lacunar resorption by osteoblasts furnished by the connective tissue is the chief factor in the absorption process, and the new bone forms in the connective tissue both by a metaplastic and a neoplastic process. Roentgenologically, osteoplastic metastasis is characterized by a finely granular, evenly distributed radiopacity, without apparent en-

largement of the bones. The femurs are frequently involved. There is no thickening of the cortex in metastasis. The early manifestations of metastasis are seen as decreased density of the bone with "spottings" of deeper density. Areas of increased density are seen most frequently in the margin of the sacro-iliac synchondrosis. These may be unilateral or bilateral. In one case in which the progress of the metastasis was noted on repeated examination, the lesion commenced in the inner margin of the right sacrum and involved the entire right side of the



Fig. 276.—Osteitis fibrosa of sclerotic type. The homogeneous density of the shadow may be noted.

pelvis before invasion of the left side, and later of the whole skeleton, became apparent.

Osteo-arthritis may involve the margins of the sacro-iliac synchondrosis, and the lower lumbar and upper sacral vertebrae, casting a shadow that may simulate closely that of early osteoplastic metastasis; when this occurs in older persons with some generalized osteoporosis due to senility, distinction may be difficult. The shadow of arthritis is finely striated and close study will show that it involves the joint and not the bone;

superimposition of the bones in this joint must always be kept in mind. Frequently additional evidence of osteo-arthritis in the spine or the hip joints will be of assistance in differentiation.

I have been interested in a series of cases in which osteitis involving the pelvic bones on one side only was revealed. Some showed the coarsely mottled shadow with multiple striæ throughout, characteristic of osteitis deformans; the patients were of the



Fig. 277.—Osteitis fibrosa, possibly syphilitic origin. The coarsely mottled shadow with suggestion of small cyst formation simulates osteitis deformans. Lack of involvement of femurs and atypical appearance of striæ suggests possible syphilitic lesion.

age at which this disease is common, and in the absence of other clinical manifestations one must designate these as probably cases of early osteitis deformans. Several other patients had localized areas of marked radiopacity, homogeneous in density, and approaching that of sclerosis. One gave a history of having had typhoid fever and, although the Wassermann test was

negative, she had had two miscarriages and one child who died shortly after birth. Two possibilities were considered, typhoid osteitis and the hyperostotic form of bone syphilis (Fig. 276). Two other patients had similar shadows in the bone and clinical evidence of syphilis (Fig. 277). One patient had had typhoid fever several years before and no clinical evidence of syphilis.

In all congenital and acquired syphilitic changes of the skeletal system there are two fundamental processes functioning simultaneously: destruction of the bone substance by syphilitic granulation tissue, and formation of new bone. It is characteristic of syphilis frequently to find the two forms in combination. Necrosis of the original bone, and also of the newly formed bone, plays an essential part in the often excessive formation of new bone. The bone necrosis exerts a powerful stimulus on the osteogenetic tissues, that is, the periosteum, endosteum, and connective tissues. The necrotic areas become surrounded and infiltrated by proliferating bone-building tissue. In this manner the newly formed bone-structure finally completely replaces the preformed dead bone. Rarefying osteitis may occur in an originally sclerotic area, leading in such a case to secondary osteoporosis. On the other hand, the originally lesser, newly formed, spongy bone in healing may become sclerotic. Many similar factors are present in typhoid osteitis, and there is evidence of this in the difficulty of distinguishing syphilitic from typhoid osteitis in flat bones, such as the clavicle.

DISCUSSION

Osteitis deformans is characterized by cortical proliferation which, when demonstrable in the femur and skull, is pathognomonic. The shadow is coarsely mottled, with multiple striæ, and occasionally evidence of cyst formation. Carcinomatous osteitis is coarsely granular, never striated, does not apparently increase the volume of the bone, and never causes cortical proliferation (Fig. 278). In radiopacities of homogeneous, sclerotic-like density, syphilis or typhoid fever may act as the primary factor. A few can only be regarded as due to osteitis fibrosa of undetermined cause.

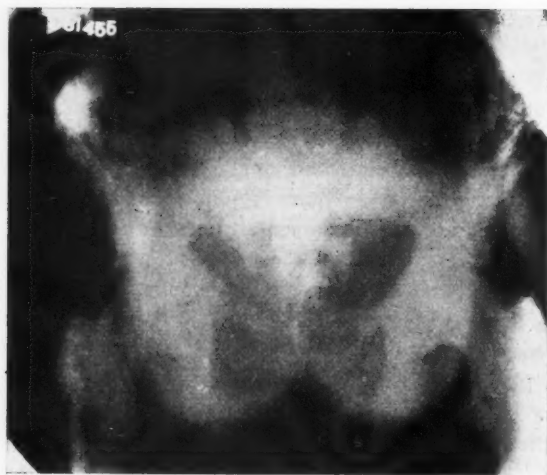


Fig. 278.—Osteoplastic metastasis from carcinoma of prostate. The fine granular appearance of the shadow and lack of any cortical thickening in the femurs may be noted.



Fig. 279.—Osteoclastic type of metastatic carcinoma. A "melted ice" appearance along the crest of the right ilium, left sacro-iliac synchondrosis, and left and right pubis and ischium may be noted.

The osteoclastic form of metastasis can best be visualized if one considers the bony structures as a cake of ice with radio-translucent areas that have been "melted" out (Fig. 279). The characteristic roentgenogram shows destruction without evidence of bone proliferation. It is most frequently seen with mammary carcinoma; hypernephroma and neurocytoma are the next most common primary causes. Combinations of the osteoclastic and osteoplastic types of metastasis are seen in a certain proportion of mammary carcinomas (Fig. 280), the majority



Fig. 280.—Combined osteoclastic and osteoplastic metastasis. On a field of generalized radiotranslucency are seen "spottings" of radiopacity. These are particularly well shown in the pubis, ischium, and femurs of both sides.

of which show widespread destruction of bone with "spotting"; rarely the osteoplastic feature is predominant (Fig. 281).

Multiple myelomas are defined as "specific malignant tumors of the bone marrow, characterized by multiple foci of origin." Roentgenographically they are apparent as numerous, widely distributed "vacuolizations" in the bone, particularly striking in the bones of the skull. Clinically, the roentgenologic data may be checked by examination for Bence-Jones protein in the

urine, but this is found only in about 80 per cent of the cases and is known to appear intermittently. Lesions considered as multiple myelomas have been found on careful search to have their source in small carcinomatous nodules in the breast, and have been reclassified as metastasis.

Gas in the bowel superimposed on the bone may simulate closely the osteoclastic type of metastasis, and opinions should be guarded in the presence of gas.

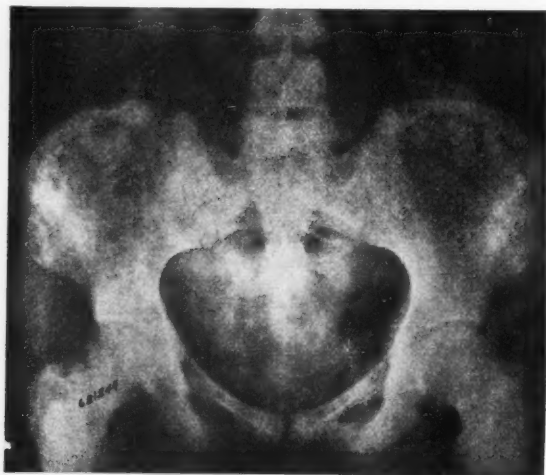


Fig. 281.—Osteoplastic type of metastasis in a case of carcinoma of the breast. Here are seen multiple areas of osteogenesis, and in the same field are evidences of osteoclasia.

Malignant tumors involving the pelvic bones are usually localized, and clinical evidence of a mass corresponding to the site of the lesion will aid in differentiation.

Osteitis fibrosa cystica, von Recklinghausen's disease, and osteomalacia are characteristic roentgenographically, and their confusion with metastasis is not probable.

THE CARE OF THE FEET IN CHRONIC ARTHRITIS

PHILIP S. HENCH AND HARRY FORTIN

PATIENTS with chronic arthritis suffer most mentally and economically when the hands and feet are involved. Arthritis of other joints may lead to serious disability, but it is with the extremities that one works and moves about. Disability of the lower extremities has a more profound effect on the psychologic state of the patient than disability of the upper extremities. Serious deformities may be present in the hands or arms of a patient, but if motion in the feet is maintained his sphere of physical activity is still wide and his spirits may be but little affected. Being a "cripple" implies primarily the inability to walk and may be attended by definite psychopathologic changes. Therefore, the care of the feet and the prevention of deformities in this area assume special significance.

Chronic arthritis may involve many joints in an inflammatory process and bear the designations infectious, rheumatoid, or atrophic. It may be confined to the weight-bearing joints (the chronic static type), without the associated systemic manifestations of infection. All joints are subjected to physiologic trauma of considerable degree by normal movements, but the weight-bearing joints carry an added burden of trauma. These joints, especially those of the feet, seem prone to arthritic involvement since loci minoris resistentiæ are produced in them by excessive physiologic trauma. Under the added stress of infection, of abnormal trauma such as results from marked obesity, or of a combination of these factors, the weight-bearing joints may be the only ones involved, or they may be the first affected and the last to heal of many involved in the process. No matter what the main etiologic factor in arthritis, trauma is often present, either as an inciting or an aggravating factor.

In the chronic traumatic or static form of arthritis, where pathologic obesity seems to be the dominant etiologic factor in the production of arthritis of the weight-bearing joints, the pathologic trauma must be removed by appropriate reduction of weight and support for the affected joints. In the infectious form of arthritis even the normal physiologic trauma of walking may no longer be well borne, and special support may be needed.

The results of infection or abnormal trauma that are most commonly associated with chronic arthritis of the feet are: (1) pronation defects; (2) depression of longitudinal or anterior transverse metatarsal arches, or both; (3) metatarsalgia and painful calluses; (4) bunions and hallux valgus; (5) "Achilles" or "calcaneal" spurs, and (6) rigid feet and toes (pes rigidus, hallux rigidus). These conditions may give rise to considerable pain and definitely aggravate the arthritis. A vicious cycle may be formed wherein the inflammation or abnormal trauma produces weakened ligaments with pronation or flattening of the feet, and the arthritis at these sites is made worse by the abnormal trauma of an incorrect, unphysiologic position. The correction of these conditions often is neglected entirely, or they are considered part of the patient's misfortune which he must bear with his main affliction. Correction, if considered at all, is too often postponed to the "orthopedic phase" of the disease.

There are two phases, generally speaking, in the progression of chronic arthritis. In the acute and early chronic stages the patient consults the general practitioner and the internist. In the late chronic and inactive stages the orthopedic surgeon is usually called to care for residual deformities. This is not a desirable situation, for the special care of the feet and the care of the systemic manifestations and focal ramifications associated with arthritis are generally worthy of the combined effort of both groups almost from the inception of the disease. Only by the early and continued coöperation of both physician and orthopedic surgeon can the progress of the disease be stopped, or at least directed so that the minimal amount of deformity may result.

The recognition of the importance of the associated dis-

turbances of the feet, their vicious nature, the symptoms they actually produce or are capable of producing, and the comparatively simple means for preventing or correcting them are, of course, among the first things that an orthopedist learns. As it is the physician who first sees such conditions a knowledge of their importance and a consideration of their treatment is a part of his responsibility in the earlier phases of the disease, but in the treatment he should coöperate with the orthopedic surgeon when possible or necessary.

In certain instances special care of the feet may give the only relief to a discouraged and otherwise disappointed patient. In the early care of these troubles the relief obtained may be so prompt and so striking that the patient may be made unusually grateful and confident, receiving a stimulus that will carry him far on the slower and longer journey to the stage of inactivity of the primary lesion.

We shall present here seven cases of chronic arthritis in which special attention to the feet afforded important support to the general treatment by removal of foci, adequate prolonged physiotherapy, nourishing, eliminative diets, vaccine stimulation, and analgesic and empiric medicines. We shall not discuss the general care aside from that for the feet.

REPORT OF CASES

Case 1. Pronation of ankles and flattening of the longitudinal arches of feet, associated with local and general chronic infectious arthritis.—A farmer aged thirty-six was admitted to the Clinic September, 1926. Eight years previously "rheumatism" in the spine appeared. Other joints have since become involved, the left ankle having become sore and swollen four months before admission.

At examination spondylitis with dorsal kyphosis, swelling, and limitation of motion of both ankles, and hydrops of the right knee were found. The ankles were pronated, and there was flattening of the longitudinal arches with considerable pain on walking. The roentgenogram of the feet showed only slight bony hypertrophy with marked bone atrophy. Except for hot baths for the entire body the patient had had no previous treatment (Fig. 282).

The feet were so swollen that correct shoes could not be worn. Baking, massage, and nonweight-bearing exercises and contrast baths for the feet were advised. The swelling gradually subsided and in four months the patient was able to wear proper shoes with corrections for the pronation and arch defects, which "helped a lot" at once. Two months later he discarded

crutches, in June, 1927 he began to work, and in November he reported that he was working full time, was very much improved and too busy to continue the physiotherapy which seemed no longer necessary.

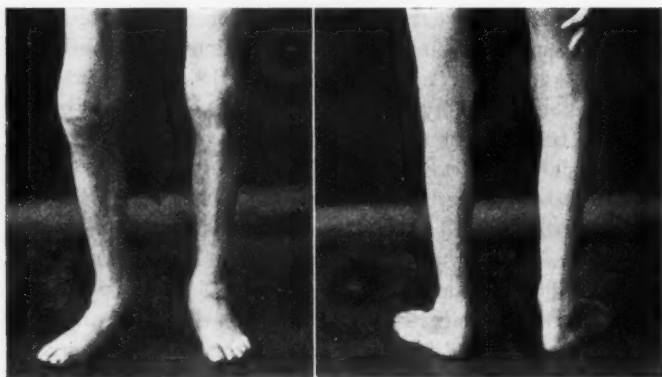


Fig. 282.—Pronation of ankles and flattening of the longitudinal arches of feet.

Case 2. Pronated ankles and flat feet with chronic infectious arthritis.—The patient, aged nineteen, was admitted to the Clinic June, 1926. In May, 1925 he began to have pain in his right ankle which he thought due to a



Fig. 283.—Pronated ankles and flat feet with chronic infectious arthritis.



Fig. 284.—Hypertrophic changes in the tarsal joints with bone atrophy.



Fig. 285.—Foot impressions appear normal, but there were definitely weakened arches.

sprain, but the pain persisted even in spite of removal of some foci. A year later there was polyarticular involvement.

No pain was present in the feet except on walking, but then it was so severe that he could walk only with great difficulty. The ankles were definitely swollen and painful (Fig. 283). They creaked on motion and there was a 30 per cent loss of motion. There was pronation of the ankles and flattening of both longitudinal arches. The feet were cold and clammy. The roentgenogram showed hypertrophic changes in the tarsal joints with bone atrophy (Fig. 284).

Although the foot impression (as it frequently may) looked "normal" and suggested an adequate maintenance of the arches, the patient experienced marked relief at once when orthopedic heels and transverse bars were applied to the shoes (Fig. 285). Physiotherapy had been instituted only a few days before and was continued; however the pain in the feet was relieved promptly as soon as the correct shoes were worn. Until the patient became accustomed to the new shoes the ankles were a bit sore, but on dismissal, three weeks after admission, he walked quite well and with very little pain.

The term "flat foot" is relative and not always a true definition of an abnormal condition. There is no one normal type of foot. Some arches are normally high, some quite low, and neither are necessarily pathologic. Foot impressions are not true aids in the diagnosis of flat foot, as many feet in which there is no pain and which function normally are quite flat with a marked areal increase in the impression, while feet which cause great pain may give normal impressions. No attempt should be made to elevate the arch if the foot is strong and active and gives no pain even though the arch is low; however, if there is pain in the foot, even if the arch is high, the foot is in urgent need of care. Indeed, when the ligaments once start to stretch, the high arch breaks down more easily than a low arch. The term "broken or depressed arch" or "weak foot" is more correct than "flat foot." Feiss defines it as a foot in which the position of the bones resembles that of the bones of the arch in physiologic weight-bearing, but which persists when the body weight is removed; and Dunn defines it as occurring in a foot in which the height of the arch is depressed more than 20 per cent.

The integrity of the individual arch is maintained largely by the compensation of the ligamentous support against body weight. Muscular support is a minor factor. When ligamentous

"decompensation" occurs, broken arches result and symptoms develop. Since the visual examination of an arch or the examination by foot impressions, or even by roentgenograms may be misleading and often productive of erroneous conclusions regarding function, subjective symptoms assume the important rôle in diagnosis. Blodgett pointed out that pain in the foot is the most important subjective symptom. In his series of 1,000 cases of broken arches, pain was absent in about 4 per cent. Pain was present only in the feet in 68 per cent, in both the feet and the lower extremities in 26 per cent, and in the lower extremities above the feet in 2 per cent. The site of the pain in cases of broken arch depends on the physiologic anatomy of the decompensating ligaments.

The chief causes of broken arches in adults, excluding neurologic lesions, are infection (local or general) and trauma from occupation or from pathologic obesity. In Cases 1 and 2 the broken arches were of the inflammatory type. A high percentage of patients with chronic infectious arthritis examined at the Clinic have pronation defects and broken arches of the type described in these cases. In most cases of infectious arthritis there is swelling of soft periarticular tissue, capsular thickening and ligamentous weakening with stretching, in the feet at least, and occasionally with contraction. The flat foot of the arthritic patient aside from the inflammation, has the usual characteristics of the ordinary nonarthritic flat foot. With arthritis, pronation of the foot at the ankle is usually the first sign of beginning ligamentous decompensation, and generally appears before lowering of the longitudinal arch. When pronation alone is present the function of the foot can be restored to normal by supination. The pronation is due to inward and downward rotation of the astragalus on the os calcis (often carrying the scaphoid with it) and the outward rotation of the os calcis, which is best seen when the patient stands with his back to the examiner and the feet parallel (Fig. 282). In the normal patient the central line of weight bearing, passing over the anterior superior spine of the ileum, extends down through the middle of the patella and over the second toe. In the

pronated foot this line of weight may pass to the inner side of the big toe or down the center of the longitudinal arch.

The patient often stands with the forefoot abducted and in walking assumes a characteristic stiff, awkward gait, with the feet turned out (Figs. 282, 283). As the normal rotary motion of the foot is accomplished by motion at the subastragaloid and midtarsal joints, pronation defects are accompanied by active and passive limitation of inversion and eversion with pain on forced motion. Dorsal and plantar flexion operate through the ankle, and are not affected by the subastragaloid abnormality of a pronation defect. The inner border of the normal foot is concave, but in the pronated and relaxed foot the inner border is convex (Fig. 282).

The degree of pain is not always proportional to the degree of pronation or of depression of the longitudinal arches. Pronation or depression which occurs rapidly causes much more distress than deformities occurring gradually, and pronation with depression is more painful than pronation alone. In the foot affected by infectious arthritis early gradual pronation alone often occurs, with depression a later and less frequent complication. The pronation places a strain on the ligaments and muscles on the inner side of the leg, chiefly the tendons of the tibialis anticus and posticus muscles. The internal malleolus and head of the astragalus become more prominent and the external malleolus less so. Consequently the chief points of tenderness and pain are along the inner side of the plantar fascia, under the tubercle of the scaphoid, at the internal malleolus, and along the subastragaloid joint line. Spasm of the peronei muscles may be associated with pain in the lateral side of the leg and calf. If patients with local involvement of the foot or general constitutional affections are confined to bed for weeks and then allowed to get up and walk in ordinary bedroom slippers or stocking feet, they often soon complain of pain in the foot which is usually of this type. The foot should be held in slight supination and should only be allowed to bear weight when leather slippers or shoes that give support to the arches are worn. Many defects of the foot could thus be prevented.

In Case 1 the pronation and depression defects were in a fairly early and active stage, with such a degree of activity that the application of the proper shoe corrections had to be postponed. Alterations for existing defects must be made gradually. At the Clinic the shoe ordinarily used has a straight last (a last with a straight inner border) and a rounded toe with a broad heel. The shank of the shoe has the additional support of a



Fig. 286.—Orthopedic shoe. Upper view: the straight last shoe; transverse bar in position proximal to the heads of the metatarsal bones. Center, the broad and almost perpendicular heel. Lower, Thomas heel.

piece of spring steel. Some patients have a rather wide forefoot and narrow heel, or a narrow forefoot and a wide heel, both of which can be fitted by a combination last. A "combination last" is one which accommodates a foot in which the normal relationship in the relative size of the forefoot and heel are disproportionate. As soon as the shoes are fitted a Thomas rubber heel (one in which the inner border extends farther for-

ward than the outer border) is applied, and the patient is urged to walk to accommodate the shoe before other alterations are made (Fig. 286). As necessary the heels and, at times, the inner side of the soles are supinated from an eighth to a fourth of an inch. When there is more pain, sole or heel-pads may be fitted in the shoes. Felt pads usually afford the most comfort, and piano-felt is used because it is firm, does not change shape on pressure, and yet is easy to mold to the necessary conformation. The pads must be fitted gradually, as too rapidly building up causes increased pain. Frequent additions to the pads can be made until the necessary support is obtained, and the foot is adapted to them.

The chief objection to the rigid arch supports so promiscuously and widely used is that they may induce atrophy of muscle by their extreme rigidity. Some of the less rigid supports afford relief, and if the patient is comfortably fitted no further alterations need be made. A high-heeled shoe, of course, creates a marked incline or slope to the foot and the weight-bearing surface is dangerously decreased. A high-arched shoe without a rigid shank allows a weak longitudinal arch to depress. A narrow, pointed shoe restricts toe motion, decreases the weight-bearing surface, increases the trauma to the heads of the metatarsals, and aids in producing metatarsalgia.

The application of correct shoes furnishes an important supplement to physiotherapy and special exercises for the feet. The contrast baths especially afford relief and should be used in addition to periodic professional and continuous home physiotherapy and exercises for the correction of the broken arches.

The simple methods of applying heat that a patient may use in his own home include especially the use of a "baking machine," a cradle of carbon lights, in the use of which he has been carefully instructed by a physician or physiotherapist. Heat can then be applied for approximately twenty minutes once or twice a day followed by certain specific exercises for the correction of the pronation and depression defects. It is difficult for the patient to apply massage himself; this should be done generally only by professional service. If electricity for a baking

machine is lacking, an apparatus which utilizes "canned heat" can be used.

In giving the contrast baths the feet and legs are placed in water as hot as bearable (about 105° F.) for about one minute, then plunged into cold water (about 45° F.) for about half a minute, and back into the warm water. Keep this up for ten or fifteen minutes, ending in the warm water.

The exercises most often used for the correction of the depression deformities are outlined in most books on orthopedic surgery. A brief outline of instructions is as follows:

Nonweight-bearing exercises.—1. Roll a rubber ball between the soles of the feet. 2. Grasp marbles with the toes, moving a number from one place to another. 3. With knees crossed drop the foot, next draw both toes and heel inward, then lift foot with heel and toes still held inward; repeat a number of times.

Weight-bearing exercises.—1. Walk with weight on the outer border of each foot, keeping feet parallel. 2. Stand with feet parallel and rise to the outer border. Return to first position without letting the arch sag. 3. Stand with feet parallel, and then separate the heels by rolling outward at the hips, at the same time rising slightly on the toes. Do not bend the knees. 4. Stand with toes projecting over the edge of step and depress toes; repeat. 5. Stand with feet parallel and elevate the toes; repeat. 6. Separate the toes a number of times.

Judgment must be used as to the amount of exercise the foot will stand. Very weak feet should first have only the exercises without weight bearing. As the feet become stronger, weight-bearing exercises can be attempted. From two to ten minutes should be spent on exercises each day.

In the infectious type of arthritis the extremities are usually cold, clammy, and at times covered with a marked film of perspiration. For hyperhydrosis of the feet a 10 per cent solution of formaldehyde may be used. Patients are instructed to wash their feet in warm water and then dry them thoroughly, after which the solution is put on and allowed to dry. This may be followed by a temporary burning sensation. The application is made once a day for three days, then discontinued until the feet begin to perspire again, when the procedure is repeated. The periods when the perspiration is controlled usually lengthen appreciably.

Case 3. Hallux valgus and severe deformity of the toes, associated with chronic infectious arthritis.—A woman aged fifty-eight had suffered from generalized infectious arthritis which, although of only two years' duration, had played havoc with many joints, producing severe arthritis defor-

mans. One of the most bothersome deformities was the marked hallux valgus of the right foot which was very painful and associated with extreme abduction deformity of the great toe, and with generalized pain and swelling of the foot. A small bunion existed in the foot before the onset of the arthritis, but it had increased in size and marked valgus deformity had appeared since the onset of the inflammatory process. The roentgenogram showed destructive arthritis in the joints of the feet and ankles, and marked abduction of the right great toe, with bunion formation.



Fig. 287.—Hallux valgus, graded 4, associated with destructive arthritis.

Hallux valgus with bunion is, of course, one of the most common disturbances of the feet, especially if there are broken arches; however, it may be particularly painful when it is associated with and influenced by destructive deforming arthritis. The results of inflammation produce lateral deviations of the toes as well as of the fingers; however, there is the necessity of fitting the deformed foot with the proper shoes. Often associated with the hallux valgus are bunions, painful bursæ over the heads of the first metatarsal joints. These deformities are often induced by narrow, pointed shoes, and stockings that are too

short. If the bunion does not cause pain a shoe that gives the forefoot plenty of room is provided. If, however, as in this case pain is severe, surgical intervention such as the Mayo operation for bunions, in which the head of the first metatarsal is removed may be necessary. It may be necessary to amputate the great toe or, more often, markedly deformed small toes.

Case 4. Achilles' or calcaneal spurs and metatarsalgia, associated with chronic infectious arthritis.—A man aged thirty-five suffered from chronic infectious arthritis which had begun seven years previously and had spread to many joints. For four years he had had difficulty and pain on walking, especially at the bottom of the right heel and in both feet at the Achilles insertion. There was no pain at the bottom of the left heel. When the patient was barefoot or wearing soft bedroom slippers, most of the pain was

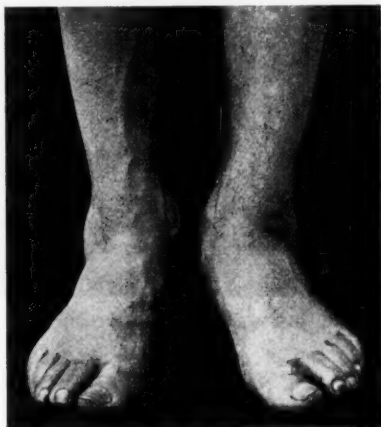


Fig. 288.—Pronation of ankles and longitudinal arches depressed.

localized in the sites mentioned, and there was also pain under the anterior arches. Ordinary shoes relieved the pain somewhat and, when the patient was not on his feet, they were practically free of pain.

All motions of the feet were diminished, swelling was present in the distal portion of the right foot at the metatarsal ridge and in the toes of the right foot. Both ankles were pronated and the longitudinal arches were depressed (Fig. 288). There was pain of the plantar fascia on pressure and when the right os calcis was compressed laterally. There was pain at the insertion of the right tendo achillis, but none on the left. Beneath the metatarsal arch a callus was beginning to form and there was definite metatarsalgia,

and tenderness under the metatarsals on pressure or on walking. The roentgenogram revealed large calcaneal spurs of both heels, roughening of the insertion of both tendo achillis and peri-arthritis of the metatarsal phalangeal joints (Fig. 289). The special treatment for the feet included the application of soft pads in the shoes, in addition to baking, massage and exercises, and contrast foot baths.

In the foot affected by arthritis there may be tenderness localized at the bottom of the heel, at the attachment of the plantar fascia, at the sides of the os calcis, or at the insertion of the tendo achillis on the os calcis. This is due to the formation of "calcaneal" or "achilles" spurs, thickenings of soft tissue associated with painful bursæ at the attachments of the



Fig. 289.—Large calcaneal spurs with roughening of insertion of both tendo achillis.

tendons. As the inflammatory thickening persists and progresses, osteogenesis from the adjacent periosteal tissue takes place and bony spurs are produced. The roentgenogram may be negative until the bony deposits occur. Pain and tenderness may be present before or after the roentgenogram is positive, and may be entirely out of proportion to the size of the bony spur. The preosteophyte stage (with negative roentgenograms) may be very painful. On the other hand, a large bony spur which causes no pain may be found as in this patient's left foot.

The etiology is varied. In infectious arthritis there may either be actual infection at these sites in the foot, or merely

undue stretching of the plantar fascia in relaxed pronated feet. This was formerly thought to be especially associated with gonorrheal arthritis; but it is now recognized that trauma, or the results of nonspecific focal infection are more frequently the cause. The spurs are often very disabling. "Calcaneal" (infra-calcaneal) spurs are much more frequent than "achilles" (supra-calcaneal) spurs. In the former the pain and tenderness is directly under the anterior portion of the os calcis at the attachment of the plantar fascia. In the latter it is at the insertion of the tendo achillis. The diagnosis suggested by the site and character of the pain may be confirmed by pressure on the heel or lateral compression of the top of the os calcis, whether or not the roentgenogram is positive.

Conservative treatment is advisable and palliative measures often are successful until the arrival of the late inactive stage, when even large bony spurs may become painless. The relief or removal of pressure from the painful areas is the chief aim. For the calcaneal spurs soft sponge-rubber pads may replace the heels of the shoes, or felt pads with a hole directly under the spurs may be inserted inside the heel of the shoe. To relieve the pressure from the side when the achilles spur is present the heel of the foot may be raised from one-half to three-fourths of an inch by inserting a felt pad in the heel of the shoe, or by strapping the foot in an equinus position to remove the friction of the shoe in walking. Felt pads placed in the shoes on either side of the painful areas may also add comfort. The local application of unguentum hydrargyri as a counterirritant may supplement heat and massage.

Surgical intervention is seldom advocated at the Clinic, for the spurs are prone to recur. Even if they do not recur the pain often persists after surgical treatment. Operation is justified and may be attempted if the spurs are excessively long and produce mechanical disturbances.

Metatarsalgia was also present in the right foot of this patient. It is usually associated, not with pronation alone, but with depression of the anterior metatarsal arch with plantar prominence of the heads of the metatarsals. Actually the anterior

arch, so-called, exists only in textbooks on anatomy or without weight-bearing, as on weight-bearing there is normally complete and painless depression of this arch and when the weight is removed from the foot the arch is at once restored. When it is continually depressed, metatarsal pain and calluses are produced. The depression of the arch makes the heads of the metatarsals prominent, and the toes become flexed dorsally. High-heeled shoes that are too short or narrow in the toe, throw excess weight on the heads of the metatarsals, producing metatarsalgia by this effect alone or in combination with inflammatory changes in the foot. As a result there may be one large pad of callus or two or three small ones under the heads of the metatarsals which may cause severe pain, especially at the third and fourth toes. The feet are fitted with shoes which allow more toe room. Transverse leather bars are fastened on the soles of the shoes just back of the heads of the metatarsals or a firm pad of piano felt is placed in the shoe, so that during weight-bearing the pressure comes first on the heel and then on the bar or pad just back of the painful area.

Case 5. Rigid foot and rigid hallux with pronation of the ankle, associated with chronic infectious arthritis.—A laborer aged sixty-one suffered from chronic, polyarticular, infectious arthritis for two or three years. On walking there was considerable pain above and below the ankles. A pronation deformity was present at both ankles with the center line of weight-bearing passing through the longitudinal arch. Inversion and further eversion were impossible; rotary motion was absent at the subastragaloid joint. The feet were swollen and there was pain when forced motion at this area was attempted. The left great toe was rigid and could not be flexed or extended: hallux rigidus. Felt pads and transverse bars were applied in the shoes and physiotherapy used.

In this case pronation defects were present, but the longitudinal arches were only slightly depressed. The rigid flat foot is a very crippling condition. The pronation and relaxation of the longitudinal arch may be extreme, and if so are usually associated with abduction of the forefoot so that the patient walks on the head of the astragalus and scaphoid bones, which usually are underlaid by painful callosities. There is a great increase in the stress in pounds for each square centimeter on

the middle area of the rigid arch, when atrophy of plantar muscles occurs from the disuse of these muscles incident to rigidity.

If the rigid foot causes no pain and the patient is able to carry on his usual labor, no interference should be attempted. If it causes pain, conservative physiotherapeutic measures are first employed, especially if any passive supination remains. If mobility is not increased by a prolonged course of heat, massage, and exercises, then manipulation under anesthesia followed by the application of casts is necessary, after which correct shoes to hold the feet in a natural position are provided. If manipulation fails, surgical intervention may be necessary. A wedge of bone is removed from the inner side of the foot in an attempt to reform the normal longitudinal arch.

Hallux rigidus may cause marked pain in the receding foot during walking, for it is then that the lack of mobility and the loss of flexion of the toes produce pain across the forefoot. Normally on walking the weight is first borne by the heel, then by the forefoot. With the final push prior to advancing the receding foot there is dorsal flexion of the toes, especially the great toe. When this is prevented by ankylosis as in hallux rigidus, the gait is altered to minimize pain. A shoe with a rigid sole will aid materially in relieving the discomfort. If these measures are unsuccessful, arthroplasty may be performed.

Case 6. Chronic traumatic (static) arthritis of the feet associated with obesity; painful heels with calcaneal spurs.—The patient was a woman aged thirty-seven, who was just at the beginning of the menopause. Until the patient was twenty her weight was normal. In the last fifteen years she had had six children, and there had been an increase in weight after each pregnancy. At twenty she weighed 130 pounds, at thirty over 200 pounds, and on admittance she was about 72 pounds overweight, being 5 feet, 4½ inches, and weighing 212 pounds. There was a degree of dyspnea and palpitation. At varying intervals for several years she had suffered from pain in the heels when walking or standing, there was swelling of the ankles and feet when the patient was on them all day. Recently she had low backache, and the feet hurt so badly when she was on them that she was unable to walk, but there was no pain when she was off the feet (Fig. 290).

Both heels were tender on firm pressure; the arches were fairly well preserved and there was no limitation of motion of the feet or ankles. The pa-

tient's knees creaked and were painful when she climbed stairs. The roentgenograms showed hypertrophic arthritis of the sacro-iliac areas, periarticular arthritis of the knees, and a small calcaneal spur on the left foot.

The patient was instructed in weight reduction and physiotherapeutic measures, and orthopedic heels and felt and rubber heel pads were applied to her shoes. Inasmuch as she was a housewife with the care of six children, it was not expected that she would be successful in obtaining relief. She returned six weeks later. She was still on her feet all day and suffered greatly. She had lost 15 pounds. The feet were strapped with adhesive, following



Fig. 290.—Chronic traumatic (static) arthritis of feet associated with obesity.

which there was immediate gratifying reduction of pain. The straps were left on for four or five weeks. Then further corrections were made in the shoes. Six months after the first admission, she was able to be on her feet all day with practically no pain. The soreness had left the knees two months before. She weighed 168 pounds. She was advised to have three infected teeth removed for local reasons.

Only the weight-bearing joints were affected in this case. The type of arthritis present has been variously called "hyper-

trophic," "osteo-arthritis," or "arthritis of the menopause." It has been thought to be due to a low-grade infection in an obese person, attacking only the joints subjected to excessive physiologic trauma which become areas of lowered resistance, and the infection does not spread generally. If it is a true infection, systemic manifestations⁴ of infection at least are entirely different from those of the so-called infectious rheumatoid type. The occasional degree of fever, low blood pressure, loss of weight, decreased appetite, secondary anemia, cold, clammy condition of the extremities, muscular atrophy, reduction of gastric acidity and sugar tolerance, and afebrile tachycardia that characterize the infectious type are all usually absent in static arthritis.

We believe that this type is not infectious, but is due to the chronic trauma of obesity. Such arthritis often occurs about the time of the menopause, probably merely because obesity of a supposed endocrine type often comes on rapidly at that time, and it occurs similarly and quite as readily in cases of early marked obesity in both men and women. To exclude an endocrine factor absolutely would be difficult, for in most cases of obesity this factor is presumably present, but the fact that the weight-bearing joints are so generally the only ones affected speaks for chronic excess physiologic trauma or "pathologic microtrauma" (as contrasted to acute or chronic gross trauma) as the cause. Static arthritis, therefore, is one of the penalties of obesity, and it is the reserve tensile strength of the ligaments and cartilages of the joints thus injured that determines the length of time between the gain in weight and the appearance of arthritis. Sudden acute obesity would be expected to lead to joint "decompensation" more readily than slowly developing obesity to which there may be accommodation at least for a number of years.

The affection seems, therefore, largely a question of abnormal statics (abnormal body mechanics); the joints usually affected being the feet or knees first, then the lumbar spine, and occasionally the hips; however, it may be confined to the lumbar spine, knees, or feet alone. The roentgenographic changes in static arthritis are either periarticular or hypertrophic, prac-

tically never destructive, and in the spine rarely extend above the second lumbar vertebra. What would seem to be a further important point in the differential diagnosis of this form from the infectious form (which, of course, may occur also in an obese person) is that even though the knees or back may be quite sore, muscle spasms about the knees or lumbar spine are not present to the degree of producing flexion deformities and kyphosis. If these occur, a primary infectious element is probably present.

With this conception of the disease and its etiology⁵ it is obvious that treatment is primarily centered on means to provide support and to relieve the abnormal trauma of obesity. Although the hyperhydrosis, muscular atrophy, and inflammatory swelling are usually absent in the feet in this type of affection the same deformities may occur as with infectious arthritis: pronation defects, broken arches, spurs, metatarsalgia, and bunions. In Case 6 calcaneal spurs were most troublesome. Dunn has estimated that the heel reaches its absolute limit of reaction against the weight placed on it when the foot is subjected to a body-weight of about 110 pounds, due to the heavy pad of dense tissue on the base of the calcaneum which can be expanded only to a definite limit. From Dunn's collection and consideration of considerable data it seems proved that a definite correlation exists between body-weights over 150 pounds and flat feet. As the body grows heavier, although the chief percentage increase is shifted to the ball of the feet, the middle or arch area of the foot still assumes the support of the greatest actual amount. The heels also share in the increase, but the actual percentage of the total weight borne by this area is decreased slightly. For example, at a body-weight of 114 pounds, approximately 18 pounds are supported by the anterior arch, 79 pounds by the arch or middle area, and 17 pounds by the heel. With a weight of 195 pounds, 42 pounds, 120 pounds, and 32 pounds are distributed to the respective areas. These relationships are altered in the abnormal foot.

One can readily appreciate, therefore, what may occur when the niceties of architectural balance are disrupted in a case of

static arthritis, first by obesity itself, then by improper shoes, and last by the vicious cycle induced by the resultant pronation and depression defects themselves. The head of the astragalus may rest on the floor with weight bearing; with knock-knee an additional burden is present, putting added strain on thigh and low lumbar muscles. Tender areas in the feet may be supplemented by fatigue pains in the arches and tender spots in the muscles of the calf.

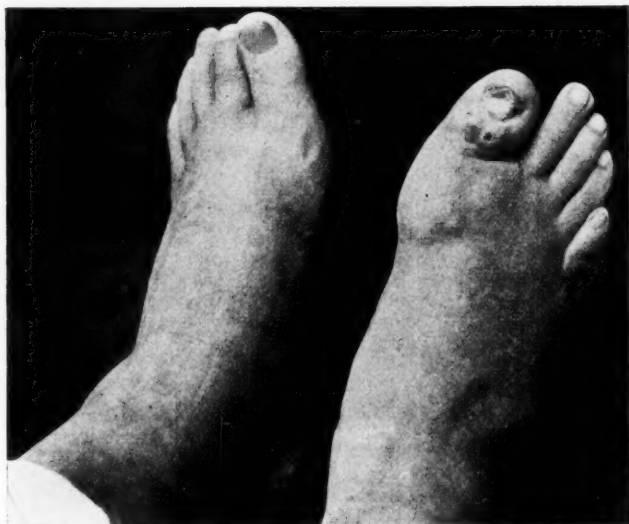


Fig. 291.—Tophaceous swellings of feet in patient with gout.

Treatment therefore includes primarily reduction of weight to as near normal as possible, proper support for the feet, afforded by correct shoes with specific alterations as indicated, with the addition of foot strapping if necessary during the period of rather acute pain. The straps are removed as soon as possible and usually shoes give sufficient support. The removal of focal infection as necessary for local reasons is probably not specific, but comes under the heading of general relief measures.

Case 7. Ulcerating tophi in the feet with depressed arches and chronic gouty arthritis.—The patient, a man aged fifty-nine, was obese. Pain first had appeared in his foot twenty-eight years previously, the day after he had worked (as a tinner) on a ladder. For three years there were semi-annual recurrent attacks of pain, swelling and redness of the right great toe and in the right tarsus. The attacks lasted about two weeks and the feet recovered completely. Then other joints became affected, and many nodular swellings appeared on fingers and toes. The attacks became more chronic and complete remissions no longer occurred, but persistent disability was present, chiefly characterized by "weak feet" which prevented him from working. Removal of foci gave no relief.

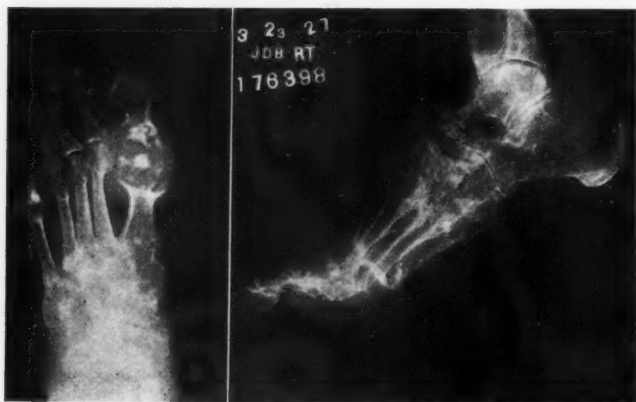


Fig. 292.—Hypertrophic and destructive arthritis associated with gout.

Characteristic gouty swelling of the great toe (right) was present. The nodular swellings were tophi, two of them ulcerating with small open sinuses at the base of both great toes (Fig. 291). There was much bony overgrowth at the right tarsus, two large irregular areas (tophi) on the dorsum of the right foot, depression of the right arch, and swelling over the dorsum of the arch with considerable pain on weight bearing. The roentgenogram showed hypertrophic and destructive arthritis with marked "punched-out" areas (Fig. 292). The blood uric acid was 6.7 mg. for each 100 c.c.

The localization of periarticular or intraarticular arthritis about the great toes is, of course, so suggestive of gout as to seem almost diagnostic, but in a large group of cases of arthritis of the infectious type the foot and even the great toes is so frequently involved that the importance of this point is often

minimized or lost sight of. Suffice it to say that during the twenty-eight years of this patient's trouble gout had never been diagnosed; it had always been diagnosed "infectious rheumatism" or "chronic arthritis." The large and small tophi might have been interpreted as rheumatic fibrous nodules, but even if they were ignored, the small periarticular ulcerations would still be characteristic of gout. Aside from the chronic sinuses of tuberculous arthritis, which are usually associated with monarticular involvement in conjunction with the characteristic inflammation, chronic arthritis of the extremities with periarticular swelling, usually asymmetrical (as contrasted to the symmetrical swellings of infectious arthritis), in which slow indolent ulcers have formed, is almost always gouty. The extensive urate deposits composing the tophus may so invade the periarticular soft tissue that necrosis occurs which ulcerates to the surface, often necessitating amputation of a finger or a toe.

Certain additional clinical data, which give adequate basis for a presumptive diagnosis of gout even in the absence of an elevated blood uric acid and tophi, have been discussed previously⁶ and are outlined by Rentschler.

The production of pronation and depression defects in gouty arthritis is much the same as in other forms, with the addition that not only the joint cartilage and part of the bone but also part of the ligaments may be actually destroyed by urate depositions. The treatment is similar to that for the other types with, of course, the all-important need for dietary correction of the purines, the dominant metabolic error. Surgical amputation of a phalanx has been mentioned as an occasional eventuality.

SUMMARY

The common deformities discussed in association with chronic arthritis of the feet may cause great discomfort, which need not necessarily be tolerated as an inevitable part of the patient's suffering. They can often be prevented, and their prevention or recognition and early care should be a part of the physician's responsibilities in the "medical phase," not in the late or "orthopedic stage" of the disease. Orthopedic consultation is very

desirable throughout the entire clinical course, but much can be done by the general practitioner without recourse to surgery. That a vicious cycle is often induced by these secondary and minor lesions should be recognized. An understanding of the rather simple mechanics of the normal foot, and the physiologic abnormalities which these deformities can produce, will lead to a comprehension of the uses of the old and simple devices described. Local physiotherapy and general treatment for the primary condition, arthritis, are, of course, measures of great importance.

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"GOUTY ARTHRITIS": THE IMPORTANCE OF PERIODICITY WITH COMPLETE REMISSIONS AS AN AID IN EARLY DIAGNOSIS

EDWIN B. RENTSCHLER

ANYONE engaged in the diagnosis and treatment of arthritis will soon realize that, although gout and "gouty arthritis" may present a classical picture which seems easy of diagnosis, the disease is often overlooked or, rather, its manifestations misinterpreted. As a result of such errors, or the delay in correcting them, the gout may progress until it has assumed chronic form characterized by such signs as tophi or the late changes in the joints revealed by the roentgen ray. In order to emphasize the sources of error and some criteria on which an early diagnosis may be made, I shall present the histories of five cases of this type of arthritis stressing the characteristic features of the clinical course and the objective evidence of the disease.*

BASIS FOR DIAGNOSIS

An absolute diagnosis of gout is made at the Clinic when the history is characteristic, and elevation of blood uric acid, or tophi, or both is present. A presumptive diagnosis of gout can often be made earlier with relative certainty on the clinical course alone, before the tophaceous stage manifests itself. A history of periodicity with complete remission is characteristic of the arthritis of gout, and is as important in the diagnosis of early gout as in the diagnosis and differentiation of peptic ulcer.

Statistics on relative frequency must be gauged by the standards of diagnosis, and must specify whether they concern

*The cases are selected from a group of cases of gout; a comprehensive clinical study of this group by Vanzant, Nomland, and Hench will be published shortly.

true gout—with or without the late manifestations, hyperuricemia and tophi, or the vague syndrome to which the term "gouty" is commonly applied. It has been considered that gout is more common in Europe than in this country, although Williamson seems to believe that it is more than twice as common in America as in any country in Europe. It is possible that the supposed greater incidence of gout in Europe depends on the difference in dietary habits there, or that the diagnosis in this country is more often made only when absolute because of the more widespread utilization of chemical studies of the blood, and that the unsubstantiated term "gouty" is, therefore, less frequently applied. The diagnosis of gout is too often made with indefinite substantiation, the term "gouty" being applied to joints not actually proved to be so. When a patient who is excessively addicted to the use of meat or alcohol happens to acquire infectious arthritis the disease is often incorrectly diagnosed gout, while a patient who is not given to excess in either may contract true gout. On the other hand, an early presumptive diagnosis can be truly made on the basis of a characteristic clinical course, and not merely on the patient's supposed "gouty habits" and the suggestive localization of the joint lesion.

REPORT OF CASES

Case 1.—A draughtsman aged twenty-five had an attack of acute pain in the ball of the foot five years before admission; the region became red and swollen, and he was unable to walk. Since then there were recurring attacks of the same sort, each lasting for from four days to two weeks, usually associated with fever and affecting most of the joints at one time or another; but until one and a half years before admission the intervals had been free from pain, and no permanent changes had occurred in the joints. Since then there had been soreness and occasional pain between attacks, and slight crippling in the fingers and great toes. The patient often experienced prodromal symptoms, such as indefinite pains in the joints, headache, and a general feeling of malaise. The attacks became more frequent and more severe, and often began at night. There was no family history of gout and the patient was not a heavy meat-eater, nor had he ever used alcoholic beverages.

The general examination was essentially negative, except for changes in the hands and feet. On the distal joints of various fingers there were several small tophi (Fig. 293); both great toes were slightly deformed, and from a tophus on the right ear (Fig. 294) sodium urate crystals were obtained.

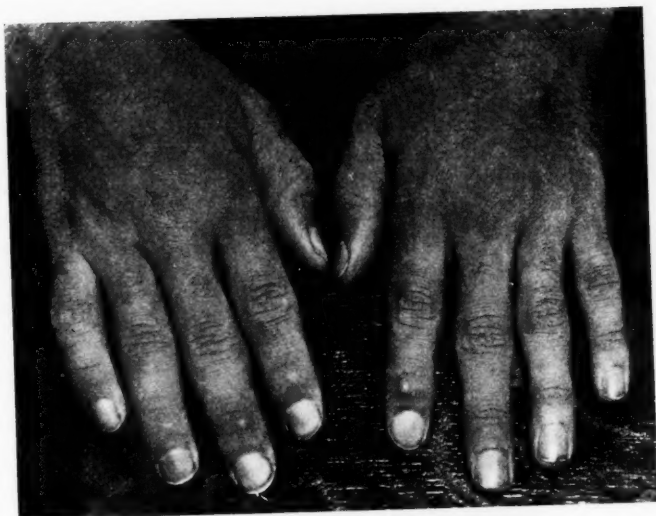


Fig. 293.—Tophi on the distal joints of the fingers.



Fig. 294.—Tophus on the pinna.

Roentgenologic examination showed destructive arthritis of the finger joints with small, punched-out areas (Fig. 295) and hypertrophic arthritis of the tarsal joints. The blood urea on admission was 50 mg., but rose during an acute exacerbation shortly after admission to 110 mg. The uric-acid content of the blood rose from 9.6 to 16 mg., and the creatinin from 2.3 to 4 mg. during the subsequent attack. The specific gravity of the urine was 1.033; albumin, graded 1, and casts, graded 2, were present. The phenolsulphonephthalein test of renal function showed 40 per cent return of the dye; a water test



Fig. 295.—Gouty changes in the joints of the finger and hand. Punched-out areas especially in the second and fifth metacarpals.

showed inability of the kidneys to dilute below a specific gravity of 1.016, and a reduction of output. A purine-free, low-protein diet was prescribed. This was supplemented during the acute exacerbation by colchicum, with heat and oil of wintergreen to the involved joints.

This case illustrates a number of the characteristic features of gout, especially the permanent injury of joints and kidney that belong to the late chronic stage. Tophi were present; the

uric acid was elevated, and tests of function showed secondary renal injury; the roentgenogram showed punched-out areas. The diagnosis was obvious in this case, but three and a half years before the characteristic history (recurring acute arthritis with complete remissions) would have warranted a presumptive diagnosis of gout in an earlier phase. It was also interesting to note that the onset was early in life, at the age of twenty, and the progress of the disease was so rapid that after five years the injury exceeded that seen in some cases of many years' longer standing.

Case 2.—A man aged fifty-eight had had a sudden attack of acute pain in the ball of the left great toe ten years before admission. The toe

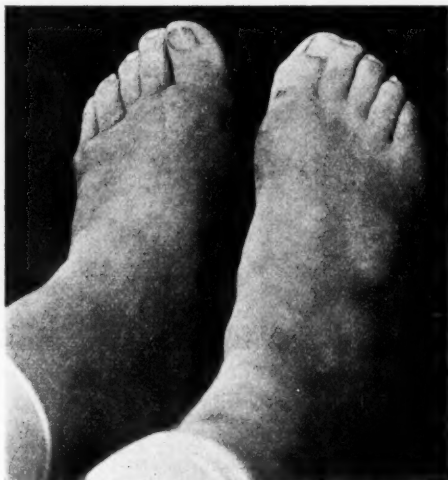


Fig. 296.—Tophaceous nodules on the feet.

became red and swollen. The onset of the initial attack occurred at night. For seven years such attacks recurred, involving the great toes or tarsal and metatarsal joints, lasting from one to four weeks. There was no pain in the intervals and the joints were apparently not grossly injured. During the last three years other joints had been affected from time to time and permanent changes had taken place in some of them.

The proximal joint of the right thumb and the proximal joints of both great toes were irregularly enlarged, and there were several large nodules on

the dorsum of each foot which were probably tophaceous (Fig. 296). A nodule removed from the left olecranon showed urate deposits.

The roentgenologic examination showed destruction of the distal end of the first right metacarpophalangeal joint and the metatarsophalangeal joints of both great toes, suggesting gout (Fig. 297). The blood urea was 31 mg. and the blood uric acid 6.1 mg.; the phenolsulphonephthalein test gave a 50 per cent return; the urine was normal except for the presence of albumin, graded 1. The water and concentration tests showed no abnormality of renal function. The patient was given a purine-free, high-protein diet, and atophan.



Fig. 297.—Destructive changes in the metatarsophalangeal joints of the great toes.

The patient was a heavy meat eater and an alcoholic habitue. The site of the first attack and the roentgenogram were both suggestive of gout; tophi were now present and the uric acid was increased. An absolute diagnosis of gout could, therefore, be readily made. But here again there was a period of seven years before the appearance of tophi or injury of the joints. From the standpoint of early diagnosis, however, the importance of the early clinical history (recurring acute attacks of arthritis with complete remissions) must be emphasized.

Case 3.—This patient, aged forty-five, first had trouble twenty years before admission. At that time a sudden acute attack of pain occurred following a baseball game and the patient could not walk. Since then there had been one or two attacks each year, lasting at first one week, later as long as four weeks. These came on suddenly and were often preceded by prodromal symptoms, such as malaise and urticaria. Most of the attacks had affected some part of the feet or hands. Until seven or eight years before admission there had been no pain in the intervals and no gross changes had occurred in the joints, but since then crippling and chronic deformity had taken place in the hands and feet and tophi had appeared. A year before admission a quantity of urates was removed from the left heel, and during the course of the last year urate deposits had been removed from the right heel as well as from the fingers. In spite of persistent treatment (continuous meat-free diet for twelve years) there had been no improvement. Recently the use of meat once a day with restriction of vegetables had effected slight improvement.

The patient was a healthy-looking man, somewhat over-weight. All joints were free except those of the hands and feet where there were small tophaceous nodes, from one of which urates were obtained. There was marked enlargement of the interphalangeal joints of the first and fourth fingers on the right hand. Roentgenologic examination revealed destruction and hypertrophy of the metatarsophalangeal joints of the great toes and of the metacarpophalangeal joints of the left little finger. The blood uric acid was 6.8 mg.; the blood urea and renal function were essentially normal. The patient was given a purine-free, high-protein diet, and atophan.

In this case also the diagnosis was obvious from the increase in blood uric acid and the presence of tophi, supporting the characteristic clinical history. In this case again there was a long period (thirteen years) during which these signs were not present, but the clinical course alone would have warranted a presumptive diagnosis of gout. The importance of this as a diagnostic factor was not appreciated, and the true diagnosis was not made until the disease had progressed for seventeen years. Although the patient was a well-developed, portly person, he did not indulge in dietary indiscretions and was a total abstainer from alcohol.

Case 4.—A man aged fifty-three six years before admission had experienced a sudden attack of pain in the left leg which came on during a hunting trip, and he had to be carried home—game, gun, and gout. Since then subacute attacks had occurred ten or twelve times a year, lasting from one to four weeks, principally affecting the hands and feet. Many of the attacks had been associated with fever and, at these times, the joints had often been red and swollen. The intervals had been entirely free from pain, and gross permanent changes

in the joints had not occurred. There was no history of tophi having been present. There was no gout in the family. The patient was not a heavy meat-eater, nor addicted to the use of alcohol.

General examination was essentially negative and there were no gross changes in the joints. The patient looked healthy and was somewhat overweight. Roentgenologic examination revealed slight periarticular arthritis of the joints of the hands and of the first joint of the great toe, but no intra-articular changes. The urine contained a trace of albumin, and the phenol-sulphonephthalein test gave a 50 per cent return. The blood urea on admission was 38 mg.; the uric acid was 6.2 mg. A purine-free diet was instituted and atophan prescribed. The case had previously been diagnosed neuritis and no mention of gout had ever been made to the patient.

In this case, aside from the increased uric acid, there was no evidence of gout except the characteristic clinical history. It is in this type of case that a presumptive diagnosis of gout is justified. In a case such as this, or more particularly in a case with such a characteristic history, even without hyperuricemia, a therapeutic test often affords added information. A high-purine diet may be prescribed for several days without medication in an attempt to aggravate pain, or a purine-free diet with colchicum may be instituted at once and relief from pain watched for. The results of these procedures may be suggestive. Certainly in case of doubt the patient should have the benefit of the doubt and should receive a purine-free diet and atophan as part of the treatment.

Case 5.—An Italian aged fifty-two had suffered a severe acute attack of pain in both thighs seventeen years before admission; this lasted one week and disappeared entirely. The second attack came one year later and was localized in the right heel and ankle. Since then there had been recurrent attacks two or three times a year, most often in the spring and autumn, lasting from one to twelve weeks. During the first five years there were no symptoms in the intervals between attacks, and no gross residual changes in the joints. Three years before admission tophi began to appear on the hands; since then others appeared on the knees and the ears. The patient had never been heavy meat-eater, but had been in the habit of drinking considerable wine. There was no family history of gout. A diagnosis of gout had never been suggested to the patient and treatment for gout had not been instituted.

The patient was a healthy-looking man, somewhat overweight. General examination was essentially negative except for changes in the joints. There were small tophi on the metacarpophalangeal joints of both hands. Both knees were irregular in contour, with large firm nodules over the anterior

aspect, and there was a flexion deformity of about 70 degrees in the left knee. Both great toes were red, swollen, and painful. Roentgenograms showed marked destructive arthritis of the joints of the hands. The blood uric acid was 6.1 mg.; the blood urea and renal function were normal.

A purine-free diet and wine of colchicum were prescribed for the exacerbation which was present at the time of admission. Later atophan was substituted for colchicum.

In this, as in Case 3, the disease had progressed for seventeen years before the true diagnosis was made. Again the patient presented the history of characteristic recurring attacks of acute arthritis with complete remission which warranted early diagnosis. During the later years the diagnosis was plainly written in the form of multiple tophi.

It is interesting that the initial attack in this case was localized in the thighs rather than in the foot. In Case 3 the pain of the onset was in the middle of the lower leg. In both of these cases, however, the subsequent attacks more often involved one or both feet, especially the metatarsophalangeal joint of the great toe, and in the remaining three cases the trouble started in one foot. Some writers have called attention to the fact that attacks are more prone to occur in the spring and autumn. This is shown only in Case 5 of the series. Pain coming on at night is believed by some to be suggestive of gout. Such a history was obtained from two of the patients.

ETIOLOGY

The subjective symptoms of gout were described as early as the seventeenth century by Sydenham. In 1860 Garrod published his classical description of the clinical manifestations of gout, and expounded his hypothesis of uric-acid retention. He attributed the retention of uric acid to failure of the kidney to excrete uric acid properly.

The work of Folin, Berglund, and Derrick in 1924 has thrown considerable doubt on the validity of this theory. They have done considerable work to show that the low output of endogenous uric acid, which is rather characteristic of gout, may be accounted for by increase in the destruction of uric acid in

circulating blood rather than by the old theory of retention. Finck contends that the hyperuricemia of acute attacks is not associated with a process of progressive retention of uric acid by the tissues, but may result from liberation from the tissues of previously retained urate excess.

One can only conclude that, although the disturbance in purine metabolism is the dominant known factor in the cause of gout, the exact mechanism and relationship are not yet known. It is commonly agreed that heredity and diet are the chief inciting causes of this disease. So far as the diet is concerned, purine-rich foods and alcoholic excesses, especially in the form of wines and beers, seem to play the leading part, although in some cases the history of these is absent.

INCIDENCE

Gout is perhaps seen more often in the fourth decade, but careful elicitation of the history often reveals onset in the early twenties. This is illustrated by Case 1 in which the first attack was at the age of twenty. In two of the cases the onset was early in the fifth decade; in one in the fourth, and in another in the third.

CLINICAL COURSE

The clinical course of gout, as far as the joints alone are concerned, seems to be quite characteristic. Clinical conceptions based on proved cases of gout, not only on the presumptive cases, and observations of a large number of cases of arthritis of all types, lead to the conclusion that recurrent arthritis which disappears repeatedly, without early signs of abnormality in the joint, should be considered either gout or rheumatic fever. In rheumatic fever the heart is usually affected at least after the second or third attack, whereas in gout, although cardiac enlargement and decompensation may occur eventually, they appear late in the course and endocarditis is not characteristic. Therefore, with such a history of recurring acute attacks, cardiac involvement speaks for rheumatic fever, and its absence for gout. Acute infectious arthritis may subside after the first

attack without residual changes in the joints, but rarely after the second or third attack does it subside completely without leaving some residue, if only in the form of a little stiffness or slight enlargement, with or without positive roentgenographic manifestation. Hench has graphically represented the comparative clinical course of these three diseases in the accompanying chart (Fig. 298).

Although the initial onset may be in other joints, gout more commonly and characteristically affects the joints of the great toe first, but acute infectious arthritis involves joints of the feet in so many cases that this localizing point is often not given

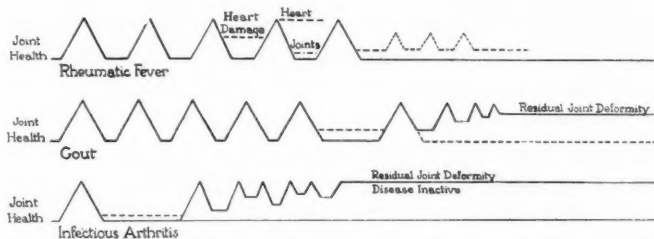


Fig. 298.—Usual course of various diseases of the joints. The peaks represent active or acute attacks; the base line, joint health.

sufficient consideration. In gout there may be acute polyarthritis with fever, so closely resembling acute rheumatic fever that the diagnosis during the first two or three attacks may remain in doubt; at a later period, however, the disease settles down to its characteristic form. It usually proceeds with recurrent attacks to its chronic form, although spontaneous recovery is not unknown. A study of the clinical course shows that when the disease continues unchecked the first permanent changes that take place are in the joints. Four of the five cases presented illustrate this in the form of destructive changes in the affected joints.

The renal tissue is the second area which may show gross permanent injury, although probably with each attack the kid-

ney suffers minutely. Two of the cases showed definite evidence of renal injury.

Osler calls attention to the fact that arteriosclerosis is often associated with the late stages of gout. Secondly the function of the heart may be impaired by resultant hypertension or sclerotic changes involving the coronary vessels. A break in compensation or angina pectoris may eventuate. It would seem, therefore, that the cardiovascular tissue is the third site of breaking down, and death may occur either from renal or cardiac disease.

ASSOCIATED MANIFESTATIONS

In the late stages there are usually associated manifestations which make the diagnosis obvious. In about 50 per cent of the cases tophi are present, although in the Mayo Clinic this has been quite rare in female patients. Tophi more often appear first on the margin of the ear or in the bursæ of the olecranon, but they may appear on the dorsal surface of the feet or the hands. From these tophi uric acid can usually be obtained in the form of uric acid crystals, sodium biurate, or calcium urate. These deposits can readily be identified by microscopic examination or a simple chemical test, the murexide test, which consists of adding concentrated nitric acid to a few particles of the deposit; heating then produces a brilliant pink color. In most cases of gout, especially in the more chronic stages, hyperuricemia is present, but the uric-acid content of the blood may be quite normal and, indeed, in some cases even below normal.

In an unpublished study, Hench and Nomland have shown that gross injury of the kidney is demonstrable in about 40 per cent of the cases of gout, as contrasted to about 3 per cent in a series of cases of infectious arthritis. The renal manifestations as described by Osler, Berglund, and Müller correspond, as far as blood and urine are concerned, to chronic glomerulonephritis without the distant and systemic manifestations such as change in the eye-grounds, hypertension, and cardiac enlargement. The blood urea may be moderately increased, the urine may show albumin and casts. The function of the kidney is dimin-

ished, as shown by the phenolsulphonephthalein test and the concentration test or water test.

ROENTGENOLOGIC DATA

The roentgenologic appearance is not characteristic but may be suggestive. Punched-out areas are often strikingly evident in gout and have been considered diagnostic of the disease, but small areas of similar appearance are also seen occasionally in infectious arthritis. Sometimes, therefore, they are only suggestive of gout; when well marked, however, they are pathognomonic. Early in its course one expects to see little more than periarticular changes with deposition of urates in the soft tissues; later hypertrophic changes appear in conjunction with destructive changes. The latter may be quite marked, and may even assume a character of dissolution suggestive of a Charcot joint.

PATHOLOGIC ANATOMY

The pathologic anatomy of the arthritis of gout has been well described by Müller. At first there is a deposition of uric-acid crystals on the superficial layer of the joint cartilage; this is followed by destruction of the cartilage and later of the bone. The destroyed cartilage and bone are replaced in part by uric-acid deposits and in part by scar tissue. The connective-tissue formation may cause stiffening of the joint, and this may go to bony ankylosis. Coincident with these changes, bony outgrowths from the epiphyses appear in the distal interphalangeal joints of the fingers. Outwardly these may closely resemble Heberden's nodes. These gouty joints usually take the form of asymmetric enlargements produced by tophi in contrast to the uniform enlargements seen in infectious arthritis as, for instance, the typical spindle-shaped deformities of the fingers in arthritis deformans. Not infrequently the periarticular and articular tophi become secondarily infected and ulceration results; this is a further suggestive sign, the importance of which is discussed by Hench and Fortin in this volume.

TREATMENT

The treatment of gout will only be touched on. Fortunately arthritis of gout lends itself fairly well to treatment. Treatment, if adequate, must be dietary as well as medicinal. There should be maximal reduction of purine intake, prohibition of alcoholic beverages, and restriction of meats because of their purine (not their protein) content. Berglund advocates a purine-free high-protein diet, because he demonstrated that with this diet more uric acid was eliminated than with the purine-free, low-protein diet. Needless to say, when the kidney is injured the protein intake would have to be proportionately limited. This is illustrated by Case 1.

In the medicinal treatment some form of colchicum is chosen; in the chronic stage, however, atophan is more desirable because of its two-fold action: it is analgesic and increases elimination of uric acid, which colchicum does not. However, Weintraud urges that, at the commencement of the administration of atophan, alkalis be given for a brief period to prevent the possible deposition of urates in acid urine in the early stage of this increased excretion. He suggests 15 gm. the first day, and from 5 to 10 gm. on succeeding days.

Graham recommends that atophan be given intermittently (three or four days on, then three or four days off) and less frequently after the blood uric acid is normal. He believes that continuous administration may produce toxic effects, and describes three cases of fatal jaundice following long-continued use of atophan. The affected part should be put to rest during the acute attack; most patients gain added comfort by the application of heat, such as by baking.

SUMMARY

The history of a case of gouty arthritis will frequently reveal the fact that the true diagnosis was not made until years after the initial attack. Five cases are presented which illustrate this fact, the earliest diagnosis having been made three and a half years after the initial attack, and, in others, not until the disease had progressed for from thirteen to seventeen years.

The usual diagnosis in such cases is "rheumatism" or "arthritis." The physician is likely to be deceived by the supposed rarity of gout or the absence of tophi, hyperuricemia, or a history of excessive use of meat or alcohol. As a rule, but not invariably, the patient is well developed, portly, and has been prone to overeat. Furthermore, it is well known that alcoholic excesses serve as an inciting factor, but it is equally true that the diagnosis is frequently obvious when no history of such excesses can be obtained. Such manifestations as tophi, gross lesions in the joint, and renal disturbance more often appear after repeated acute attacks, and characterize the chronic form of this disease. Their appearance should be prevented as far as possible, and in some cases could be prevented if an early diagnosis were made and the proper treatment instituted.

In these early cases, in the absence of the contributory evidence afforded by such characteristic manifestations, the clinical history is of paramount diagnostic importance.

A history of periodic acute arthritis with complete remissions is so characteristic of gout as to be of prime importance in the early diagnosis; in diagnostic significance such oscillations are comparable to those that mark the course of peptic ulcer. Furthermore, this is often the only means by which an early diagnosis can be made.

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SYPHILIS OF THE CENTRAL NERVOUS AND CARDIO-VASCULAR SYSTEMS IN HUSBAND AND WIFE

PAUL A. O'LEARY

EVIDENCE accumulated during the last few years from the reports of various laboratory investigations of syphilis supports the original contention of Levaditti and Marie, Nichols and Hough, and Reasoner of the existence of specific strains of *Spirochæta pallida*. Besides the observations made on laboratory animals, clinical reports have appeared from time to time, calling attention to the fact that there are strains of *Spirochæta pallida* having special affinity for nervous tissue, the skin, or the cardiovascular system. I do not believe that clinical evidence supports this conception of the specificity of various strains of *Spirochæta pallida*. In my own practice examples of neurosyphilis or cardiovascular syphilis in husband and wife are not rare; more common, however, are examples of syphilis in a vital structure, such as the aorta or the nervous system, in only one of the marital partners.

A review of the clinical evidence presented by 200 husbands and wives, all of whom showed indisputable evidence of syphilis, does not reveal parallel involvement in the central nervous or cardiovascular systems as often as it is reported in laboratory animals that were infected by the same strain of organism. Study of these 200 husbands and wives showed that in 20 per cent all the tests on the spinal fluid of husband and wife were negative, and in 22 per cent they were positive. In 44 per cent it was noted that the husband presented evidence of neurosyphilis and the wife did not. In the remaining 14 per cent of the series the tests of the spinal fluid on the wives were positive, and the husbands showed no evidence of neurosyphilis clinically or serologically. This series includes only those cases in which there was evidence that either the husband or wife had been infected after marriage. The status of the spinal fluid

was used as an index of involvement of the central nervous system in all cases which did not show clinical signs of neurosyphilis. The type of neurologic involvement is not pertinent to this discussion.

Fifty-five of the husbands and their wives had undergone special examination of the cardiovascular system for evidence of syphilitic disease. In 75 per cent of the series husband and wife did not present evidence of cardiovascular syphilis, while in 10 per cent the wife presented clinical signs of aortic involvement and the husband's examination was negative, while in 5 per cent the husband's examination was positive for signs of cardiac disease of syphilitic origin and the wife's negative. In 10 per cent both husbands and wives manifested evidence of cardiovascular syphilis.

Another group of patients included members of the same family who were infected from different sources, including sisters infected by their husbands, brothers infected from different concubines, fathers and sons both with proved infections of varied origins, as well as mothers and sons with acquired syphilis. The number of cases in this group, although smaller than in the series of husbands and wives, did not offer evidence in support of the theory of specificity of strains.

A third series of 100 husbands and wives was studied, in which only the husband or the wife showed evidence of syphilis. This group does not throw any additional light on the question of the specificity of the *Spirocheta pallida*.

The occurrence of both neurosyphilis and cardiovascular syphilis in husband and wife is rare and, therefore, should not be stressed as evidence in favor of the conception of specific strains of *Spirocheta pallida*. If either neurosyphilis or cardiovascular syphilis were found in the greater percentage of the cases in husband and wife, such cases of neurosyphilis and cardiovascular syphilis would be considered an additional point in favor of the concept of specificity. The recognition of cardiovascular syphilis and neurosyphilis in the same patient is not unusual if careful examination of the cardiovascular system is made in each syphilitic patient. In fact, the frequency with

NEUROSYPHILIS WITH GROSS EVIDENCE OF SYPHILIS OF THE AORTA IN
HUSBAND AND WIFE

Group 1

<i>Husband</i> , aged forty-eight. Syphilis acquired in June, 1903. Married in 1905.	<i>Wife</i> , aged forty-seven. History of syphilis denied. Married in 1905. Pregnancies, two. Miscarriages, two.
Admitted to Clinic, May 20, 1923. General examination revealed syphilitic aortitis with aortic insufficiency and parenchymatous neurosyphilis.	Admitted to Clinic, June 5, 1923. General examination revealed syphilitic aortitis with aortic insufficiency and meningolymphovascular type of neurosyphilis.
Blood Wassermann test (Kolmer) 44 (strongly positive). Cerebrospinal fluid Wassermann test 41 (positive), Nonne positive, 31 cells, colloidal benzoin 000 000 000 000 000.	Blood Wassermann test (Kolmer) 44 (strongly positive). Cerebrospinal fluid Wassermann test 44444 (strongly positive), Nonne positive, cells 17, colloidal benzoin 002 200 333 320 000.
Treatment (May 25, 1923 to November 1, 1927): Eighteen intravenous injections of arsphenamin; five intraspinal injections of arsphenamin; fifteen intramuscular injections of mercury succinimid; ten intramuscular injections of sulpharsphenamin; seventeen intramuscular injections of bismuth; 240 mercurial inunctions.	Treatment (June 10, 1923 to November 1, 1927): Twenty-eight intravenous injections of arsphenamin; seven intraspinal injections of arsphenamin; forty-five intramuscular injections of mercury succinimid; 240 mercurial inunctions; a course of malaria therapy.
Result: The blood Wassermann test reversed to negative; cerebrospinal fluid reversed to negative in all factors; central nervous system became asymptomatic; cardiovascular system showed continued progression in the electrocardiographic readings, with increased evidence of myocardial injury.	Result: The blood Wassermann test still positive; cerebrospinal fluid Wassermann test still positive; central nervous system now showing clinical signs of paresis; cardiovascular system showed definite improvement in the electrocardiographic readings (asymptomatic).

which these complications are recognized in the same patient varies in proportion to the diligence with which the clinical investigation is carried out. The results from such clinical surveys approximate 50 per cent, while at necropsy approximately 80 per cent of the cases of neurosyphilis also show gross evidence of syphilis of the aorta.

NEUROSYPHILIS IN THE WIFE ONLY

Group 2	
<i>Husband</i> , aged sixty-three. Penile chancre had occurred in February, 1919.	<i>Wife</i> , aged fifty-nine.
At the Clinic July, 1919, syphilitic alopecia and a few recurrent papules on the prepuce were noted; Wassermann test on blood positive; Wassermann test on cerebrospinal fluid negative; Nonne test negative, 5 cells.	At the Clinic July, 1919, a maculopapular syphilid of one month's duration was noted; the patient came because of paralysis of the right side of the face and right eyelid, and severe headaches and vomiting; Wassermann test on blood positive; Wassermann test on cerebrospinal fluid negative; Nonne test positive, 24 cells; gold sol 0000000000.
Treatment: Twenty intravenous injections of arsphenamin; 230 mercurial inunctions.	Treatment: Twenty intravenous injections of arsphenamin; 264 mercurial inunctions.
Result: Wassermann test on blood reversed to positive after being negative for five years; Wassermann test, Nonne test, and cell count on cerebrospinal fluid remained negative.	Result: Wassermann test on blood and all factors in the spinal fluid were reversed to negative and remained so.

In 58 per cent of the marriages in which the same strain of *Spirochata pallida* was involved, either the husband or the wife acquired neurosyphilis. It was noted that the husbands acquired symptomatic or asymptomatic neurosyphilis four times as often as the wives, a point which has frequently been noted by syphilographers. At present there is a controversy as to

whether pregnancy is one of the factors in reduced incidence of neurosyphilis in women. Group 2 calls attention to the occurrence of neurosyphilis in the wife, while the husband's nervous system was not invaded.

The converse of Group 2 is more frequently observed, however: the examples in which neurosyphilis developed in the case of the husband, while the wife did not show signs of neurologic involvement, comprised 44 per cent of the cases studied. Group 3 emphasizes not only this point, but also the fact that the nervous system may become involved at the time of the generalization of the *Spirochæta pallida*.

NEUROSYPHILIS IN THE HUSBAND ONLY

Group 3	
<p><i>Husband</i>, aged thirty. Married in 1915. Syphilis acquired in May, 1919. Syphilis recognized as macular syph- ilid.</p>	<p><i>Wife</i>, aged thirty-one. Married in 1915. Syphilis acquired in July, 1919. Syphilis recognized as grouped follic- ular lesions with condyloma lata and mucous patches.</p>
<p>At the Clinic Wassermann test on blood strongly positive; Wasser- mann test on cerebrospinal fluid negative; Nonne test positive, 137 lymphocytes.</p>	<p>At the Clinic Wassermann test on blood strongly positive; Wasser- mann test on cerebrospinal fluid negative; Nonne test negative, 3 cells.</p>
<p>Treatment (over nine months): Treatment started on basis of sec- ondary lesions; sixteen intraven- ous injections of arsphenamin; four intraspinal injections of ar- sphenamin; 110 mercurial inunc- tions.</p>	<p>Treatment: Treatment started on basis of sec- ondary lesions; eighteen intraven- ous injections of arsphenamin; 154 mercurial inunctions.</p>
<p>Result: Wassermann test on blood reversed to negative; Wassermann test on cerebrospinal fluid negative at end of two years; Nonne test negative, 1 lymphocyte; cardio- vascular examination negative in 1925; neurologic examination negative in 1925.</p>	<p>Result: Wassermann test on blood reversed to negative; Wassermann test on cerebrospinal fluid negative at end of two years; Nonne test negative, 2 cells; cardiovascular examination negative in 1925; neurologic examination negative in 1925.</p>

Therapeutic results offer additional evidence in support of the contention that individual resistance is more potent than the strain of *Spirocheta pallida* in determining the type of syphilitic involvement. It is to be borne in mind that a certain percentage of neurosyphilitic persons spontaneously arrest the progress of the disease. This is more frequently noted in tabes dorsalis than in any of the other parenchymatous forms of neurosyphilis. No estimates have been made as to the percentage of neurosyphilitic persons in whom this phenomenon of spontaneous "cure" occurs, and it is evident how difficult an evaluation of this sort would be. The response the patient shows to modern

NEUROSYPHILIS WITH THERAPEUTIC RESPONSE SATISFACTORY IN WIFE
AND UNSATISFACTORY IN HUSBAND

Group 4

<i>Husband</i> , aged forty-two. Married in 1909. Syphilis acquired in 1915; treatment by "mixed treatment" and five injections of neo-arsphenamin.	<i>Wife</i> , aged thirty-nine. Married in 1909. Syphilis acquired in 1915, but ignored.
At the Clinic June, 1924, parenchymatous neurosyphilis, probably early paresis, was diagnosed; Wassermann test on blood strongly positive; Wassermann test on cerebrospinal fluid very strongly positive; Nonne test positive, cells 91, polymorphonuclears 20; colloidal benzoin 002 320 333 333 000.	At the Clinic June, 1924, asymptomatic neurosyphilis was diagnosed; Wassermann test on blood strongly positive; Wassermann test on cerebrospinal fluid strongly positive; Nonne test positive, cells 136; colloidal benzoin 000 000 333 320 000.
Treatment: In spite of routine therapeutic measures, clinical signs of paresis occurred one year later; after a course of malaria complete remission occurred which lasted for almost two years.	Treatment: Twenty-four intravenous injections of arsphenamin; forty-six intramuscular injections of succinimid; forty intramuscular injections of bismuth; eighty mercurial inunctions.
Result: Patient has been recommitted to the insane asylum.	Result: Wassermann test on cerebrospinal fluid negative three years later; Nonne test negative, 3 cells, patient asymptomatic.

methods of antisyphilitic treatment may be considered one method of interpreting the mechanism of resistance, and it is unfortunate that this method offers only presumptive evidence. If this view is accepted, Groups 4 and 5 are examples of the beneficial effect of treatment in the person manifesting resistance to the disease.

NEUROSYPHILIS WITH THERAPEUTIC RESPONSE SATISFACTORY IN HUSBAND
AND UNSATISFACTORY IN WIFE

Group 5

<i>Husband</i> , aged thirty-seven. Syphilis acquired in 1906. Married in 1907.	<i>Wife</i> , aged forty-two. Married in 1907. Inconclusive history of syphilis one year after marriage.
At the Clinic March, 1917, tabes dorsalis was diagnosed; Wassermann test on cerebrospinal fluid strongly positive; Nonne test positive, 21 cells; zone I gold curve.	At the Clinic April, 1927, tabes dorsalis was diagnosed; Wassermann test on cerebrospinal fluid strongly positive; Nonne test positive, 5 cells; zone II gold curve.
Treatment: Eighteen injections of arsphenamin; 220 mercurial inunctions; forty intramuscular injections of mercury succinimid.	Treatment: Forty-two injections of arsphenamin; twenty intraspinal treatments; thirty injections of tryparsamid; 440 mercurial inunctions; sixty intramuscular injections of mercury succinimid.
Result: Wassermann test on cerebrospinal fluid five years after admission negative; Nonne test negative, 1 cell; arrested tabes dorsalis.	Result: Wassermann test on cerebrospinal fluid five years after admission strongly positive; Nonne test positive, 5 cells; zone I in gold curve; progressive signs of clinical paresis.

Another group of patients, in which clinical evidence points to the supposition of resistance rather than of specific strains constitutes cases of husband and wife, in one of whom the nervous system is involved while in the other the cardiovascular system is involved. In a group of fifty-five husbands and wives, in which examination of the cardiovascular system and tests of

the spinal fluid were carried out, 18 per cent showed aortitis in one member and neurosyphilis in the other.

NEUROSYPHILIS IN HUSBAND AND CARDIOVASCULAR SYPHILIS IN WIFE

Group 6

Husband, aged thirty-six.
Syphilis acquired in 1910.
Married in 1913.

At the Clinic, May, 1923, parenchymatous and meningeal neurosyphilis was diagnosed; cardiovascular examination negative; Wassermann test on cerebrospinal fluid strongly positive; Nonne test positive, 41 lymphocytes; zone I in colloidal benzoin curve.

Treatment:

Eighteen injections of arsphenamin; eight intraspinal treatments; fifty-five intramuscular injections of mercury succinimid; twenty intramuscular injections of bismuth; thirty intravenous injections of sodium iodid.

Result:

Patient died in July, 1924 from pneumonia; no evidence of cardiovascular syphilis at necropsy.

Wife, aged thirty-eight.
History of syphilis denied.
Married in 1913.

At the Clinic May, 1923, early syphilitic aortitis was diagnosed; Wassermann test on cerebrospinal fluid negative; Nonne test negative, 5 cells; zone II in colloidal benzoin curve.

Treatment:

Eighteen injections of arsphenamin; 200 mercurial inunctions; fifty intramuscular injections of mercury succinimid; ten intramuscular injections of bismuth.

Result:

After four years of observation Wassermann test on cerebrospinal fluid negative; Nonne test negative, 1 cell; Wassermann test on blood negative; neurologic examination negative; cardiovascular examination showed objective and subjective improvement.

The study of acquired syphilis in members of the same family offers a commentary on this discussion. In another study of members of the same family who acquired syphilis from various sources, definite evidence was found that the soil rather than the strain of the organism determines the issue. It is admitted that a study of acquired syphilis in members of the same family does not produce evidence against the concept of

specific strains of the *Spirochæta pallida*, but rather emphasizes the fact that in certain families the nervous system as well as the cardiovascular system is more susceptible to injury from toxic factors. The type of the soil in which the *Spirochæta pallida* is sown is more important in determining the type of syphilis than is the strain of the organism.

An example of this point is shown in Group 7, of sisters infected from different sources and both showing unfavorable response to treatment.

SISTERS INFECTED WITH SYPHILIS FROM DIFFERENT SOURCES

Group 7

<p>Woman, aged thirty-five. Married in 1912 (at age of twenty-two). No history of primary or secondary syphilis.</p>	<p>Woman, aged thirty-three. Married in 1909 (at age of eighteen). Primary lesion in 1910, followed by secondary lesions.</p>
<p>At the Clinic parenchymatous neurosyphilis was diagnosed; Wassermann test on blood strongly positive; Wassermann test on cerebrospinal fluid strongly positive; Nonne test positive, 23 cells; colloidal benzoin 003 000 332 000 000.</p>	<p>At the Clinic exophthalmic goiter and tabes dorsalis were diagnosed; Wassermann test on blood strongly positive; Wassermann test on cerebrospinal fluid strongly positive; Nonne test positive, 17 cells; colloidal benzoin 023 322 333 100 000.</p>
<p>Treatment (in two and a half years): Twenty-four intravenous injections of arsphenamin; eight intraspinal treatments; thirty injections of tryparsamid; thirty-three intramuscular injections of mercury succinimid; eighteen intramuscular injections of bismuth; twenty injections of bichloridol.</p>	<p>Treatment (in two and a half years): Twelve intravenous injections of arsphenamin; six intraspinal treatments; ten injections of tryparsamid; thirty intramuscular injections of mercury succinimid; twenty intramuscular injections of bismuth.</p>
<p>Result: Wassermann test on blood still positive; Wassermann test on cerebrospinal fluid still positive; no change in clinical observations, although persistently positive tests on cerebrospinal fluid suggests unfavorable outcome.</p>	<p>Result: Clinical signs of paresis developed while patient was under treatment.</p>

DISCUSSION

A series of cases is presented in which husband and wife were infected with syphilis, but whose clinical manifestations did not support the contention that there are specific strains of *Spirochæta pallida* that have special affinity for the cardiovascular and nervous systems. These patients were selected from a group of 200 husbands and wives who had been observed and treated for syphilis in the Mayo Clinic for at least two years. It is not assumed that this group of patients represents the entire evidence to be offered against the theory of specificity of strains, but it is presented because syphilis of the cardiovascular and nervous systems comprises most of the late complications of the disease. The incidence of combined symptomatic and asymptomatic neurosyphilis in the Mayo Clinic (as estimated by Stokes) varies from 65 to 78 per cent. This incidence is somewhat higher than that reported from other clinics, owing to the fact that late syphilis is more frequently observed in the Mayo Clinic than the acute forms, and also because in all cases at least one examination of spinal fluid is carried out. It is worthy of note that while in 22 per cent both the husband and wife presented evidence of neurosyphilis, in 20 per cent neither husband nor wife presented evidence of neurosyphilis.

The evidence presented here indicates that the burden of proof of the existence of specific strains of the *Spirochæta pallida* remains with the advocates of this conception, and that the data accumulated from the study of syphilis in animals are not substantiated by clinical observation.

There are undoubtedly other factors, such as the virulence of the strain of the *Spirochæta pallida*, and local areas of reduced resistance, as well as general disease and trauma, that are potent in determining the course of the infection, and which must not be lost sight of in an attempt to evaluate a clinical review such as this. It is unfortunate that a clinical study of this kind offers only presumptive evidence.

THE TREATMENT OF ERYSIPELAS WITH ANTITOXIN

FRANK N. ALLAN AND RUSSELL M. WILDER

ERYSIPELAS, once an almost regular accompaniment of surgical operations, became relatively rare with the introduction of surgical asepsis. A few cases still occur, particularly after operations about the head. When the operative field is infected to start with, as is so frequently the case in operations for mastoiditis, sinus disease, epithelioma, and other surgical affections of the head, erysipelas occasionally appears to be unavoidable. Other cases follow scratches or abrasions, or originate in septic diseases of the nose, throat, or ears, and other inflammatory conditions of the skin. Erysipelas is no longer considered a contagious disease in the sense that it is communicated through the air; some abrasion, trifling or otherwise, is probably always responsible for the infection.

The seriousness of the condition is illustrated by the large experience of the Bellevue Hospital, where the mortality rate in 15,277 cases treated during the last twenty-three years was 10.1 per cent. If the erysipelas is limited to the head it is usually less dangerous; if it migrates to the trunk, the mortality percentage doubles or trebles. In the very young and very old the disease is usually fatal. If patients are hard drinkers, or if they are suffering from diabetes it is always extremely serious. Idiopathic erysipelas (medical erysipelas) carries, as a rule, a more serious prognosis than erysipelas developing after surgical operations.

Until the advent of the specific serum prepared by Birkhaug there was no internal treatment for the condition. Nonspecific vaccines and serums were tried. General measures were used as for other febrile diseases and symptoms were met as they

arose. Local sedatives and astringents of various kinds were applied; ichthyol in particular has been popular, being usually applied diluted with vaseline, as a salve. Wet dressings of strong magnesium sulphate solution have been soothing and somewhat analgesic. Wet dressings of alcohol and boric acid solution have been acceptable to the patients. Also various procedures have been designed to wall off the infection, such as intracutaneous injections of antiseptics, collodion barriers and others, but none of these measures has been of any great value. Dr. Harlow Brooks once made the cryptic comment that, whereas there are any number of methods of treating erysipelas that would make the condition worse, there had been nothing in his experience that helped it. This, we believe, has been the usual opinion.

It is particularly gratifying, therefore, to learn that the antitoxin prepared by Birkhaug, and announced by him in 1926, has proved so effective that it is now being used at the Bellevue Hospital to the exclusion of all other methods of treatment. Symmers and Lewis of the Bellevue staff recently reported their results with unconcentrated serum in 131 cases. In this series seven deaths from all causes occurred (a mortality rate of 5.3 per cent), whereas in a series of 107 cases treated without antitoxin during a corresponding season the year previously the mortality from all causes was 11.2 per cent. Moreover, the period of disability of the patients recovering was reduced 50 per cent.

Birkhaug himself had employed the serum in sixty cases at the time he made his report. This is not the first antistreptococcus serum to be made, nor the first attempt to prepare a specific antitoxin for use in the treatment of erysipelas. Birkhaug mentions Charrin and Rogers who prepared an antistreptococcus serum in 1895 and obtained a striking result with it in a case of puerperal fever. Since then numerous other investigators have considered the possibilities of specific antitoxin for use in streptococcus infections, particularly with noteworthy success in scarlet fever; Lavender, and Goresco and Popesco, also mentioned by Birkhaug, have used erysipelas antistreptococcus serum and obtained with it results that were encouraging.

Birkhaug's study first led to the conclusion that the strains of hemolytic streptococci isolated from erysipelas almost always belong in one antigenic group and differ in their antigenic properties from strains obtained from scarlet fever, cellulitis, empyema, and other streptococcus infections. He then demonstrated that intracutaneous inoculation of streptococci from cases of erysipelas in man produces a characteristic erysipelas-like lesion in the skin of the rabbit, and that mixture of immune erysipelas serum with the organisms protects the skin from this lesion. Normal serum or previously heated immune serum had no such action. He further showed that the toxic filtrate of the erysipelas strains of streptococci produces a lesion in the skin of susceptible persons similar to that produced in the Schick and Dick tests, and that this lesion does not appear if the skin-test dose (0.1 c.c. of a 1 : 1,000 dilution of the toxic filtrate) is mixed with antistreptococcic serum (0.001 c.c.).

The method of preparation of the antitoxin for clinical use was that followed by Dochez in work with scarlet fever antitoxin, the horse being immunized not only with the filtrable toxin but also with the organism.

Our own experience with this antitoxin dates from April, 1926, when Dr. John F. Anderson of E. R. Squibb and Sons kindly supplied us with a few therapeutic doses of concentrated serum. Since then we have used this preparation in twenty-two cases, the severest in a total of thirty-eight cases of erysipelas treated in the isolation annex of St. Mary's Hospital, Rochester, from April, 1926 to October, 1927. The milder cases and those already recovering at the time of transfer to the isolation annex have not been treated with the serum. In seven of the twenty-two cases receiving the antitoxin there was no appreciable effect, or the benefit was questionable. Four of these patients were treated late, that is, four days or longer after the onset of erysipelas. In the remaining fifteen cases there was definite evidence of benefit within from twenty-four to forty-eight hours after the first injection. The advance of the lesion was arrested, erythema and edema subsided, the temperature fell, and the toxic symptoms cleared. In eleven cases

the improvement was dramatic; in four cases it was less striking and yet sufficiently apparent to convince critical observers.

The cases in which the benefit from antitoxin was most evident were those for the most part in which it was given early, that is, before the end of the third day after the onset of the disease, but a case treated as late as the ninth day is also included in this group.

Thirteen patients received only one therapeutic dose, eight had two doses, and one had three doses. We believe that more serum might have been used to advantage in some of the seven cases mentioned, in which there was not appreciable benefit from the treatment given.

The usual method of administering the antitoxin is by deep intramuscular injection. Symmers and Lewis now employ intramuscular injections exclusively. At the outset they tried intravenous injections, and in five cases the results were "little short of wonderful." In the sixth and seventh cases, however, there was severe anaphylactic shock, and one of the patients died with cyanosis and pulmonary edema. They believe, therefore, that the intravenous use of antitoxin is not only unnecessary in most cases but is dangerous.

We have used intramuscular injections exclusively except in four late cases in which the lesion was advancing with great rapidity. In these we supplemented the intramuscular injection with an intracutaneous "barrier" infiltration along the margin of the lesion, a procedure that has been recommended by Rivers and Tillett, and by Musser. The result in each case was highly gratifying and we believe that this procedure should be considered whenever the result from the initial intramuscular injection is unsatisfactory. A serious objection to it is that the intradermal injections are painful, particularly when the lesion is on the face.

Our observations with the antitoxin are too few to supply statistical proof of its value, particularly in view of the well-known facts that erysipelas is self-limited and that, like many other infectious diseases, it tends to vary considerably from season to season and from year to year. Nevertheless, it is hard

to believe that there would have been no mortality in the last nineteen months, as is the case, had we not had the serum for use in the more severe cases. One patient aged eighty survived, and three infants, the youngest two and a half months of age, also recovered. In three cases the lesion involved the trunk extensively by the time the first injection of serum was made. In ten cases the erysipelas was idiopathic or cryptogenic in origin.

CASES OF ERYSIPELAS IN ISOLATION

Year.	Cases.	Deaths.	Mortality, per cent.	Average period in hospital, days.
1919.....	13			15.7
1920.....	31	6	19.4	12.4
1921.....	22			15.0
1922.....	20	1	5.0	16.7
1923.....	19	1	5.3	13.5
1924.....	27	6	22.2	8.0
1925.....	23	5	21.7	11.2
1926 Jan.-Mar.	11	3	27.3	13.8
Apr.-Dec.	18			9.6
1927 Jan.-Oct.	20			11.3
Total	204			
Before use of serum.	166	22	13.5	13.2
Since use of serum..	38*			9.7

* Twenty-two patients who had severe symptoms received erysipelas antitoxin. Four of these were also treated with roentgen rays.

The tabulation shows the mortality percentage and average period in hospital of 204 cases, treated in the isolation annex

of St. Mary's Hospital from 1919 to October, 1927. From January, 1919 to April, 1926, 166 of these cases were treated by various nonspecific measures; there were twenty-two deaths, an average mortality rate of 13.5 per cent. Since April, 1926, when the antitoxin became available, there have been no deaths; furthermore the average duration of the time in the hospital has been reduced from thirteen and two-tenths days to nine and seven-tenths days.

Platou and Rigler have recently reported unusually beneficial results in erysipelas from treatment by roentgen rays; Harbinson and Lawson have also reported favorable results by that method. Three of twenty-two patients treated with serum had received roentgen-ray treatment before transfer to isolation. In the first of these, a case of severe facial erysipelas, the roentgen-ray treatment was given on the second day of the disease. The temperature remained unchanged. The patient was very toxic on the third day and the lesion continued to spread. Antitoxin was given on the third and fourth days. The temperature fell promptly and remained normal after the fourth day. In the second and third cases roentgen-ray treatment was given on the second day of the disease, and antitoxin on the second and third days, both patients recovering after the fourth day. In a fourth case, that of a child, a small (inadequate) dose of antitoxin was administered on the third day. The temperature fell and the rapidly advancing lesion was arrested. Two days later the temperature rose and, since no more serum was available at the time, roentgen-ray treatment was given. It did not completely arrest the progress of the disease, although the child subsequently recovered.

It is impossible to pass judgment from this small experience on the effectiveness of roentgen-ray treatment. Further observations of this method are being conducted. Illustrative cases in which antitoxin was used with evident benefit are the ones given below.

Case 1.—A man aged fifty-five underwent a series of operations for restoration of the nose following resection for carcinoma. Five days after the last operation he fell ill with chills and fever, and the left cheek became

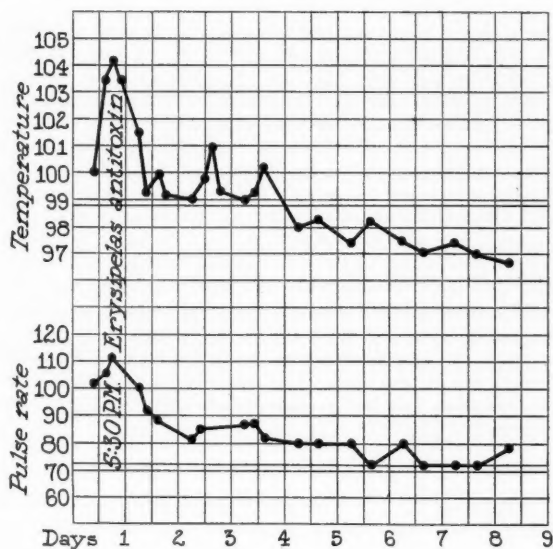


Fig. 299.

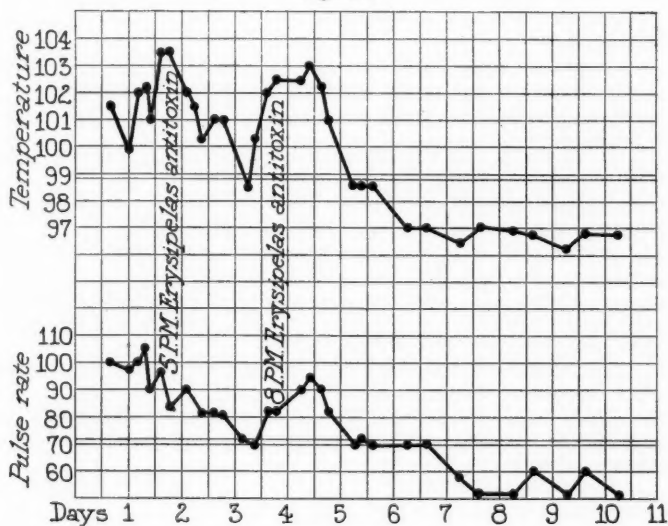


Fig. 300.

red and swollen. When admitted to the isolation hospital the following day, he was toxic and had a temperature of 104.2° F. A dose of erysipelas antitoxin was given soon after admission. The following day the temperature had fallen, the lesion had faded, and there was marked subjective improvement. Subsequent recovery was uneventful (Fig. 299).

Case 2.—A young man aged twenty-seven fell ill four days before admission to isolation with headache and a slight chill. Two days after this a tender swelling was noted behind the left ear, so that mastoiditis was suspected by the examining physician. When admitted, the swelling had extended to the left temporal region and to the neck and erysipelas was quite evident. He was toxic and the temperature was high. Following the injection of a dose of erysipelas antitoxin there was slight improvement, but the lesion continued to spread across the forehead. On the seventh day serum was injected intracutaneously along a line across the forehead above the eyebrows and back to the ears on both sides. The lesion did not advance beyond this line and by the following day had subsided. Subsequent convalescence was rapid and uneventful (Fig. 300).

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UNDULANT FEVER: THREE CASES

THOMAS B. MAGATH

It is difficult to determine whether or not certain diseases are increasing. Medical knowledge has increased and the accuracy of diagnostic methods has been so improved that the less common diseases are being more frequently recognized. This is particularly true of undulant fever. From the number of cases that are being reported today as compared with ten years ago, one might conclude that the disease is increasing rapidly in the United States. However, a careful study of the facts shows that the reason for the increase is the ability of the medical profession to recognize the condition. It is quite evident that undulant fever is and has been a fairly common disease in the United States, especially in rural districts.

Case 1.—A man aged thirty-five years had lived all of his life on a farm on which he raised a variety of domestic animals. He had been well until three months previously when he began to ache, lose appetite, and suffer from general debility and distinct feverishness. At the end of a week when he consulted a physician the temperature was 101° F., and the possibility of typhoid fever was considered. Three negative Widal tests were obtained. He remained in bed at his home for four weeks during which time the temperature varied from normal to 105° F., being as he said "up and down." He was taken to the hospital, and a diagnosis of typhoid fever made on the basis of an enlarged spleen and leukopenia and fever. He was in hospital for six days. His temperature was normal on the first day, and on the day he left it was 104° F. This came down to normal in a few days, but again rose and remained high. The patient had never drunk goat's milk, but drank milk from some of his cows that had aborted.

On examination he was found to be well nourished; the spleen was definitely palpable below the costal margin and was soft. The liver seemed slightly enlarged. The systolic blood pressure was 114, the diastolic 74, the pulse rate was 120, and the temperature 100° F. The urine was normal except for a slight amount of albumin. The hemoglobin was 77 per cent, erythrocytes numbered 4,480,000, and the leukocytes 6,200. The lymphocytes were 45 per cent, large mononuclears 3.5 per cent, transitionals 6.5 per cent, neutrophils 44.5 per cent, and basophils 0.5 per cent. The Wassermann test was negative, two cultures of the blood were negative. Examination

of the stool did not show organisms of the typhoid group, but *Endamaba coli* was found. Widal tests performed in the laboratory and at the State Board of Health Laboratory were negative. Roentgenograms of the chest were negative, and a small axillary node which was removed and examined showed inflammatory reaction. Sputum was not obtained for examination. The blood serum when tested against *Brucella melitensis* and *Brucella melitensis* var. *abortus* showed an agglutination reaction in 1:600, the absorption agglutination test showed that the antibodies were formed against the variety *abortus*, and the diagnosis was made of undulant fever.

The patient returned home, and after several weeks of debility recovered completely.

Case 2.—A farmer aged forty-two living in Nebraska came to the Clinic because of loss of weight, a tired feeling, a dry cough, and slight fever. A physician had said that he had tuberculosis and he had been resting for the last few weeks. He had been ill for six weeks. He stated that two of his cows had aborted six months previously, and that he had been drinking a great deal of milk from the cows on his farm. There was nothing else important in the history.

The patient seemed well but had lost slightly in weight. The systolic blood pressure was 116, the diastolic 78, the pulse rate was 92, and the temperature 98.8° F. Teeth and tonsils were infected. He had a right femoral hernia. The urine was normal. The hemoglobin was 70 per cent, erythrocytes numbered 4,490,000, leukocytes 7,500, lymphocytes were 35 per cent, large mononuclears 1 per cent, transitionals 5 per cent, neutrophils 58.5 per cent, basophils 0.5 per cent. The Wassermann reaction on the blood was negative. Cultures of the blood and Widal tests were negative. The blood serum showed agglutination with *Brucella melitensis* 1:160, *Brucella melitensis* var. *abortus* 1:320. The electrocardiograph revealed sinus tachycardia and roentgenograms of the chest were negative. The diagnosis of undulant or Malta fever was made.

Case 3.—A man aged thirty-one came to the Clinic because of soreness in the back and fever. He runs a stock farm in Texas. About five weeks previously he noticed that he was having afternoon fever and some sweating at night. His back was sore, he had lost about 20 pounds in weight, and he had coughed for about three weeks, but it was nonproductive. He had had a chill a few weeks before and had been taking things easy for about a month. His physician stated that he had had intermittent fever ranging from 99° to 103° F. and that his prostate was enlarged and tender, but that agglutination reactions for typhoid and Malta fever were negative. The patient stated that there had been many cases of infectious abortion in his region and that one of his cows had aborted the previous year. He had been drinking from 2½ to 3 quarts of milk a day from this cow since that time.

On examination the patient seemed to be well nourished. Aside from a systolic murmur nothing was noted in the chest. The spleen was palpable below the costal margin, he had a varicocele of the left testicle, and the prostate was soft and boggy. The systolic blood pressure was 100, the dias-

toxic 70, the pulse rate 114, and the temperature 101.4° F. The urine was normal. The hemoglobin was 75 per cent, erythrocytes numbered 4,440,000, and leukocytes 7,500. The lymphocytes were 19.5 per cent, large mononuclears 5.5 per cent, transitionals 2.5 per cent, neutrophils 72 per cent, and eosinophils 0.5 per cent. No malaria plasmodia were found. The Wassermann test on the blood, two blood cultures, and the Widal tests were negative. Agglutination test with *Brucella melitensis* var. *abortus* and *Brucella melitensis* gave a positive reaction in at least 1 : 320 dilution; absorption test showed that the organism involved was of the variety *abortus*. Examination of the stool did not reveal members of the typhoid group, and *Giardia lamblia* and *Endolimax nana* were found. Roentgenograms of the chest, sinuses, and urinary tract were negative. The patient was observed in the hospital for six days; the temperature varied from normal to 101° F., and was distinctly of the intermittent type. A diagnosis of undulant or Malta fever was made.

The patient returned to his home, and letters from his physician indicate that he is doing well and is gradually recovering.

Like many other diseases, Malta fever dates back to the time of Hippocrates, but it was not until 1878 that British medical officers established the disease as a definite clinical entity and distinguished it from malaria with which it had been confused. Bruce discovered the organism in 1887 and the agglutination reaction was introduced by Wright and Semple in 1897. Early in the twentieth century it was demonstrated that goats act as the natural reservoir for the infection. Bruce's description of the disease indicates that it is of long duration; there is continuous fever, profuse perspiration, frequent relapses, constipation, rheumatic and neuralgic pains, swelling of the joints, and congestion of the spleen. The presence of *Brucella melitensis* in the blood establishes the diagnosis. The wave-like type of fever gives it its name of undulant fever, and the fact that it was reported commonly in Malta has caused it to be referred to as Malta fever.

Craig reported the first case of Malta fever in the United States in 1905. The only epidemic that has been reported in the United States was that which occurred in Phoenix, Arizona, in 1922, and it was from material obtained then that Dr. Alice Evans began her splendid contributions to this subject. She has shown that *Brucella melitensis* and *Brucella melitensis* var. *abortus* cannot be distinguished culturally and morphologically, and that the serum of patients suffering from this disease may agglutinate both organisms. They can be separated only by

an absorption agglutination test. It is, therefore, evident that a close relationship exists between the organism of the Malta fever of goats and the *Brucella melitensis* var. *abortus* of cattle and hogs. They both produce diseases in man which are clinically indistinguishable. Evans has collected and summarized twenty cases in which the disease was caused by *Brucella melitensis* var. *abortus*. The diagnosis of the disease rests primarily on the clinical history, the presence of an enlarged spleen, the high mononuclear count, the specific agglutination reaction, and the exclusion of such diseases as tuberculosis, endocarditis, typhoid fever, and febrile Hodgkin's disease. The duration of the disease is usually long but fortunately the mortality is low, the disease is extremely debilitating, usually keeps the patient from work for from two to three months, and relapses are very common.

Although the source of infection has not been definitely proved, there seems to be little doubt that man is infected from contact with cattle or hogs which have an *abortus* infection. Perhaps the disease is obtained by drinking the raw milk from such cattle. From a long series of tests at the Mayo Clinic Hardenbergh and I concluded that 4 per cent of persons in rural districts have a positive agglutination reaction to this organism. The explanation is offered that these persons have been subjected to small numbers of the organism over a long period of time, not sufficient to produce the disease but sufficient to cause a positive agglutination reaction. For this reason it is evident that the diagnosis of Malta fever must not be made on the agglutination reaction alone. If the organism is recovered from the blood, as rarely happens, the diagnosis is evident, but failing this, in the presence of a positive agglutination reaction, the clinical history and clinical data must be relied on in making the diagnosis. Absorption agglutination tests with *Bacterium tularensis* should be made, since some cases of tularemia appear not unlike undulant fever and this organism is often agglutinated by the patient's serum in cases of undulant fever.

No specific treatment has yet been devised and one must rely on the basis of the symptoms presented in the treatment of patients with undulant fever. The ultimate prognosis is good.

ABDOMINAL MIGRAINE; MELANOMA; PELLAGRA; HEPATOLENTICULAR DEGENERATION (WILSON'S DISEASE)

LEE W. POLLOCK AND CLIFFORD J. BARBORKA

ABDOMINAL MIGRAINE

THE abdominal crisis of migraine was discussed by Liveing (1873) as a periodic seizure, beginning at any hour of the day or night without recognized cause. The pain began as a dull, bearable, rather deep, ill-defined uneasiness in the epigastrium. It increased steadily in severity and varied in duration from a few hours to several days and then decreased. It might or might not be preceded by or associated with cephalic migraine. Later writers have discussed abdominal migraine as periodic attacks of sudden, deep-seated epigastric pain associated with pressure, fullness, eructation, and occasionally with vomiting, the patients having been subject to periodic attacks of migraine all their lives.

Case 1.—A man aged fifty-four had had cephalic migraine for years. His mother had had migraine. Mild gastro-intestinal symptoms of nausea were associated, but vomiting seldom occurred. During the last year the headaches had been less severe, but abdominal distress was outstanding. It began acutely as dull, deep-seated epigastric pain, gradually increasing in severity; on two occasions morphin was required. At times pain radiated to both sides of the upper part of the abdomen and to the supraclavicular space. The patient would recover spontaneously and be perfectly well in the intervals between the attacks. He was never jaundiced, and there were no urinary symptoms.

The general physical examination was negative. The systolic blood pressure was 142, the diastolic 88; the blood Wassermann test was negative. The hemoglobin was 76 per cent, erythrocytes numbered 4,560,000, and leukocytes 6,400. The differential count, the urinalysis, roentgenograms of the chest, spine, stomach and colon, and the roentgenogram by the Graham-Cole technic were negative.

Inasmuch as a positive diagnosis could not be made exploration was performed. The stomach, duodenum, and gallbladder were normal. The entire intestinal tract was found to be collapsed, and all the intestinal organs lay deep in the pelvis. The intestinal loops were entirely collapsed, probably due to intestinal stasis, but there were no signs of mechanical obstruction. The appendix, which was removed, showed slight evidence of old chronic disease, probably of no consequence. The patient recovered uneventfully, was dismissed from the hospital, and was up and about when he was again seized with an attack. At this time, with the history and negative exploration, we felt justified in making the diagnosis of abdominal migraine.

Buchanan has stated that 75 per cent of 1,335 patients were operated on from one to seven times for the relief of migraine without beneficial results. In two cases of suspicious abdominal migraine observed during the last two years, we advised the ketogenic diet such as we are using in the treatment of idiopathic epilepsy. However, conclusions could not be drawn from the data obtained. In this case, however, because of the negative exploration, the diagnosis of abdominal migraine was fairly certain. The patient remained under supervision in the diet kitchen where he was taught the principles of the ketogenic diet.

The ketogenic diet consists of large amounts of fat with minimal amounts of protein and carbohydrate. The object of the diet is to produce ketosis as evidenced by acetone and diacetic acid in the urine. The state of ketosis is produced whenever there is incomplete combustion of fat. As long as there is 1 gm. of carbohydrate available for 4 gm. of fat, fat is completely burned to carbon dioxid and water. If the ratio of 1 : 4 is increased to 1 : 5, the fats are incompletely burned, and acetone bodies are excreted in the urine. Large amounts of acetone and diacetic acid may be excreted in the urine (which thus provides a means of insuring the correct composition of the diet) for months or even years without untoward symptoms.

Nine months have elapsed since this patient was placed on the diet, and the abdominal pain has disappeared entirely, as have the severe headaches. This case calls attention to a number of important points. Abdominal migraine, although uncommon and not discussed in most textbooks, is perhaps not rare, yet great care must be taken in analyzing a diagnosis of

abdominal migraine; organic disease as well as reflex pain from other regions must be carefully excluded. When this has been done, probably the most significant factor, from the diagnostic viewpoint, is the association of the common manifestations of the migraine characteristics with the attack of abdominal pain. It would be impossible to differentiate the abdominal crises of migraine in the absence of a personal or family history of migraine. We do not claim that the ketogenic diet is specific for cephalic or abdominal migraine, but the results from the use of the diet in this case are worthy of discussion. At present we are carrying on further research along these lines.

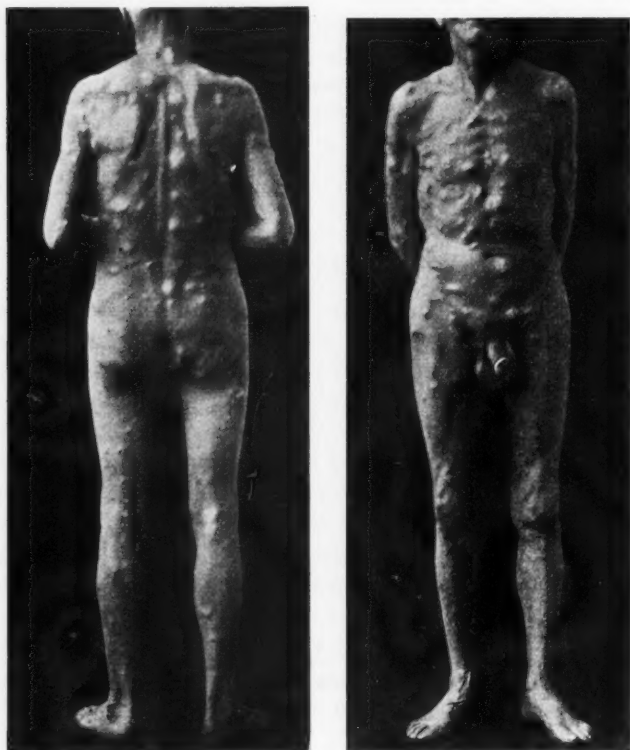
MELANOMA

Melanoma is a virulent form of malignant disease because of the early date at which it forms secondary deposits in the lymph nodes and internal organs. It grows from those portions of the body that are naturally pigmented, especially the choroid coat of the eye and the skin. Melanoma of the skin usually develops from pigmented moles into a slaty, bluish or blackish tumor. In such a case the tumor may be round, smooth, or oval, varying in size from 0.5 to 2.5 cm. or larger, or it may be irregular papillomatous tissue, horny, blackened plate, such a lesion as one would expect from the enlargement of a black mole.

Case 2.—A man aged sixty-five gave a history of having had a pigmented mole excised from the right arm six years previously, following an injury to the arm. The resulting incision was slow in healing. Two and a half years later a lump appeared in the left side of the neck. This was excised. It returned immediately, and soon lumps began to spread over the face, neck, head, arms, trunk, and legs. During the two weeks prior to examination marked jaundice developed. A generalized aching sensation and pain were experienced when the lumps were bruised.

General physical examination revealed multiple nodules over the body (Figs. 301, 302). The liver was enlarged and the patient jaundiced. The systolic blood pressure was 122, the diastolic 62. The blood Wassermann test, the blood count, and the differential smear were negative. Urinalysis did not reveal melanin, but revealed definite bile. Roentgenograms of the chest showed bilateral metastasis to the lower lobes. Excision of a metastatic nodule from the left forearm was pronounced melano-epithelioma.

This case is an unusual example of generalized metastatic melano-epithelioma. The late development of metastasis is also significant.



Figs. 301, 302.—(Case 2.) Unusual example of generalized metastatic melano-epithelioma.

PELLAGRA

Pellagra is a definite disease, the etiology of which has not been finally determined. The symptoms and lesions of pellagra are, of course, well known, although in the northwestern part of the United States the disease is not common. Except for a few

sporadic cases the disease did not occur in the United States until about 1907, when Searcy reported an epidemic of acute pellagra developing in a hospital for colored insane in Alabama. Since this report the disease has become an important problem, especially in the Southern States where it has been prevalent in such institutions as insane hospitals and in cotton-mill villages. With the recent Mississippi Valley flood disaster, many more cases of pellagra are coming to the attention of the medical profession.

The case of pellagra presented here is classical. The prodromal stage constitutes a vague, indefinite digestive disturbance, typical skin manifestations, and finally definite mental disturbance.

Case 3.—A woman aged thirty-one gave a history of having had pneumonia in March, 1923. Shortly after recovery from this illness rather vague, indefinite epigastric distress and discomfort developed. She ate less on this account and gradually began avoiding various foods. In about a year she was almost fasting, her diet consisting of bread and occasionally fruit; she drank large quantities of coffee. Gradually she noticed that her hands were dry and hard, and that the skin peeled. Next, the face and neck began to be affected, and finally the feet showed evidence of scaling, and were purplish and edematous. Associated with this gradual change in the skin she noticed some dizziness, paresthesia, muscular weakness, headache, and pain in the back of the neck. Her original weight was 123 pounds; after a gradual loss over a period of three years, she weighed 80 pounds. Symptoms of depression and stupidity followed closely, and questions were answered very slowly.

General examination revealed an emaciated, apathetic woman with a fixed gaze and facial expression. Symmetrical lesions were distributed on the backs of the hands and wrists. The face and neck were erythematous and covered with large, flaky scales. Lesions were characterized by dull red pigmentation, well defined borders, desquamation, and hyperkeratosis, which gave a dirty appearance. The tongue was glossy, redder than normal but not painful. There was moderate edema of the legs. The abdomen was normal. The systolic blood pressure was 112, the diastolic 80; the Wassermann test of the blood was negative. The hemoglobin was 65 per cent, erythrocytes numbered 4,390,000, and leukocytes 6,900. The differential smear was normal. Urinalysis was negative. The stools were negative for parasites and ova, and there was no growth of *Monilia candida*. A test-meal showed total acidity 44, with free hydrochloric acid 24. Roentgenograms of the stomach, chest, kidneys, ureters, and bladder were negative. Proctoscopic examination revealed a slightly reddened mucosa but was otherwise negative. There were no signs of cord involvement, the mental picture being chiefly that of depression with reduced psychomotor activity.

The patient was placed on antipellagra diet, and at the end of two months the dermatitis had practically disappeared. She gained 18 pounds, and gave every evidence of improvement both physically and mentally.

In discussing this disease we stated that the cause of pellagra is unknown. The relation to the continuous eating of damaged corn has long been recognized, and poverty, poor hygienic surroundings, and exposure to the sun's rays have been given as predisposing factors. There are two definite views with regard to the cause: one that food is responsible, the other that it is some form of infection, the nature of which is not known. Even those who believe in the infectious nature of pellagra admit the importance of adequate nutrition in prevention and cure.

The treatment in this case consisted of a high-calorie diet, milk, eggs, fresh beef, and leafy vegetables, such as spinach, cabbage, and lettuce. Forced feeding must be guarded, however, if there is diarrhea. Highly milled grains should be avoided. If anorexia prevails, the administration of food by a stomach tube may be necessary. In the mentally affected, institutional care is essential.

HEPATOLENTICULAR DEGENERATION (WILSON'S DISEASE)

Wilson (1912), under the title of progressive lenticular degeneration, first described a series of cases of extrapyramidal disease in which cirrhosis of the liver was associated with injury of the lenticular nuclei. Since then many other cases have been reported in which there was cirrhosis of the liver with associated nervous lesions but in which the clinical symptoms differed somewhat from Wilson's picture. Barnes and Hurst suggested that the term "hepatolenticular degeneration" be adopted, as it indicates that the lenticular lesions is a sequel to hepatic injury, and is of the type of progressive degeneration. Without hepatic cirrhosis, a case cannot be considered progressive lenticular degeneration. The nature of the disease, whose manifestations are primarily nervous, although hepatic cirrhosis is a constant and cardinal feature, is not known. Two views have been discussed: (1) that the lesion is an expression of a congenital

defect of the nervous system, and (2) that it is acquired and probably toxic in nature. The symptoms of the disease are bilateral involuntary movements of the upper and lower extremities, peculiar tremor, muscular rigidity with contractions in the advanced stage, dysarthria and dysphagia, muscular weakness and emaciation, rather marked emotional instability, cirrhosis of the liver and, in a few cases, enlarged spleen.

Case 4.—A woman aged twenty-six dated the onset of trouble to October, 1924, when she began to notice a peculiar tremor of the upper extremities. Within three months she noticed that the lower extremities had become affected. The tremor was increased by excitement or with voluntary movements, and disappeared during sleep. There seemed to be some muscular rigidity and a feeling of muscular weakness. Gradually all of these symptoms increased, and in the last year marked emotional instability had become manifest. She was sometimes irritable and then happy, and finally sorry because of her irritability.

The patient weighed 182 pounds. The systolic blood pressure was 110 and the diastolic 78. The only other observation of note was the discovery of a definitely enlarged and palpable spleen, and of a palpable liver with firm and rounded margin which could be felt only under the costal margin. Urinalysis of a twelve-hour specimen showed 500 c.c. with specific gravity of 1.022, acid reaction, and a trace of albumin. There was no sugar; microscopic examination was negative. The hemoglobin was 80 per cent (Dare), the erythrocytes numbered 4,660,000, and the leukocytes 7,200. The Kolmer modification of the Wassermann test on the blood was negative. Vision was 6/6 in both eyes; pupils, pupillary reflexes, visual fields, and fundi were negative. The patient read fine print at normal distance. With the slit lamp there was neither a "golden glow" to the iris, nor the so-called Kayser-Fleischer ring in the cornea. The iris was blue and showed fine deposits of brown pigment. Stereoscopic roentgenograms of the head were negative. Tests of hepatic function were negative.

The neurologic examination revealed peculiar tremor of the right upper and lower extremities, most intense when at rest. There was no "pill rolling" supination. While the tremor appeared constant in the upper extremity it seemed to be transient in the lower extremity, possibly as a result of changing posture. The toes of the right foot were maintained in a position of plantar flexion; they could, however, be voluntarily turned upward. There was considerable increase in tone in the right calf, with corresponding decrease in speed.

A lumbar puncture was performed December 29. Six cubic centimeters of clear colorless fluid, under 13 cm. pressure, was removed. There was prompt response to jugular pressure. The Kolmer modification of the Wassermann test on the blood was negative; the Nonne test was negative, and there was one small lymphocyte. The Lange and the benzoin curves were normal.

The type of bilateral tremor in the upper and lower extremities, muscular rigidity, emotional instability, and the hard, firm, palpable liver, certainly point to hepatic lenticular degeneration. This case, although primarily a problem for the neurologist, is presented to call the internist's attention to an affection of comparative rarity but with distinctive features so that in his chance contact with disease of the basal ganglia he may be on the lookout for associated cirrhosis of the liver and, thus, for the possibility of hepatolenticular degeneration.

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